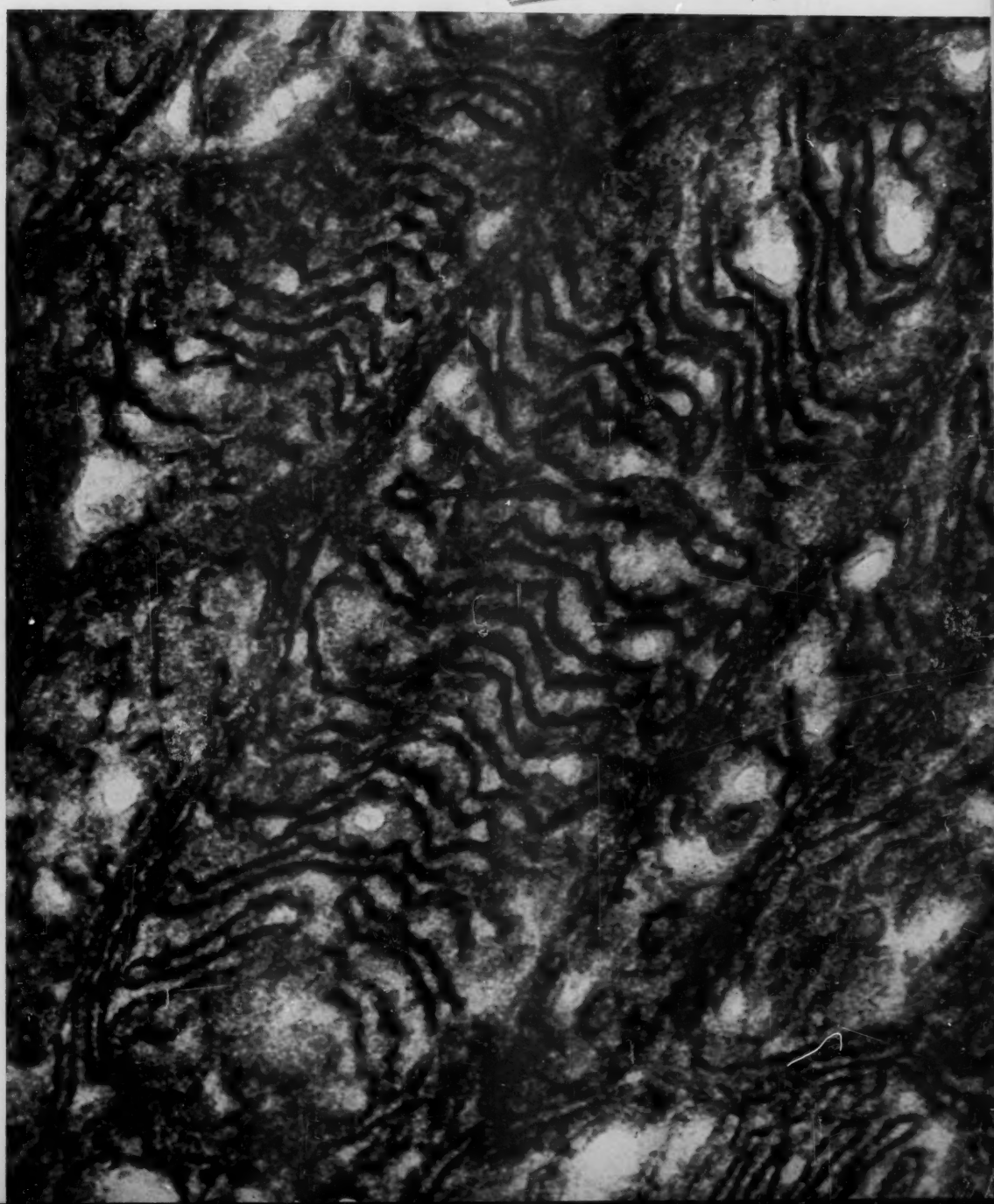
Sci. Bill.

SCIENCE

6 January 1961
Vol. 133, No. 3445

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

Jan. 25/61



For photomicrography and simultaneous observation, binocular photo tube "FS" is available

the laboratory microscope which fulfills research requirements

Model S 48/76

the new LEITZ LABOLUX IIIa

The Leitz Labolux IIIa is a new laboratory microscope with built-in illumination and the famous Labolux ball-bearing focusing control, which combines both coarse and fine focusing in a single knob. Available with a wide variety of accessories, the Labolux IIIa is recommended for all routine laboratory work and, in addition, can be equipped to fulfill the most exacting research.

A variety of interchangeable tubes is available: monocular, binocular or trinocular (binocular viewing plus photo tube for photomicrography). Tubes can be rotated 360° so that the Labolux IIIa may be faced away from the observer, for increased accessibility to all controls and to the object stage, and to make "conference-viewing" by two consultants more convenient.

Among the condensers available are the Abbe type, the Berek 2-diaphragm condenser, and condensers for phase contrast and dark field observations. The Labolux IIIa is readily adapted to fluorescence microscopy by addition of the Leitz fluorescence accessories. The large stand, in a new contemporary design, is constructed for a lifetime of use with fatigue-free operation and precision performance. All controls, including the knobs for the mechanical stage, are in a low convenient position. High-power objectives have spring-loaded mounts for prevention of damage to lenses and slides.

LABOLUX IIIa, Model S 25/95

• inclined binocular tube S with knurled knob to adjust for proper interpupillary distance • built-in mechanical stage #25 • two-lens condenser #95 • substage unit with rack and pinion focusing accepts sleeve-type condensers • quadruple nosepiece with achromats 3.5X, 10X, 45X and 100X oil immersion, the last two having spring-loaded mounts • paired 10X wide-field eyepieces • horizontal carrying case • 3-step transformer, 6 V., 2.5 Amp.

For literature and/or a personal demonstration in your laboratory, write Dept. SC-16

Leitz

E. LEITZ, INC., 468 PARK AVENUE SOUTH, NEW YORK 16, N. Y.
Distributors of the world-famous products of
Ernst Leitz G. m. b. H., Wetzlar, Germany—Ernst Leitz Canada Ltd.
LEICA CAMERAS · LENSES · PROJECTORS · MICROSCOPES · BINOCULARS

SCIENCE is published weekly by the AAAS, 1515 Massachusetts Ave., NW, Washington 5, D.C. Second-class postage paid at Washington, D.C., and additional mailing office. Annual subscriptions: $8.50; foreign postage, $1.50; Canadian postage, 75¢.

6 January 1961, Volume 133, Number 3445

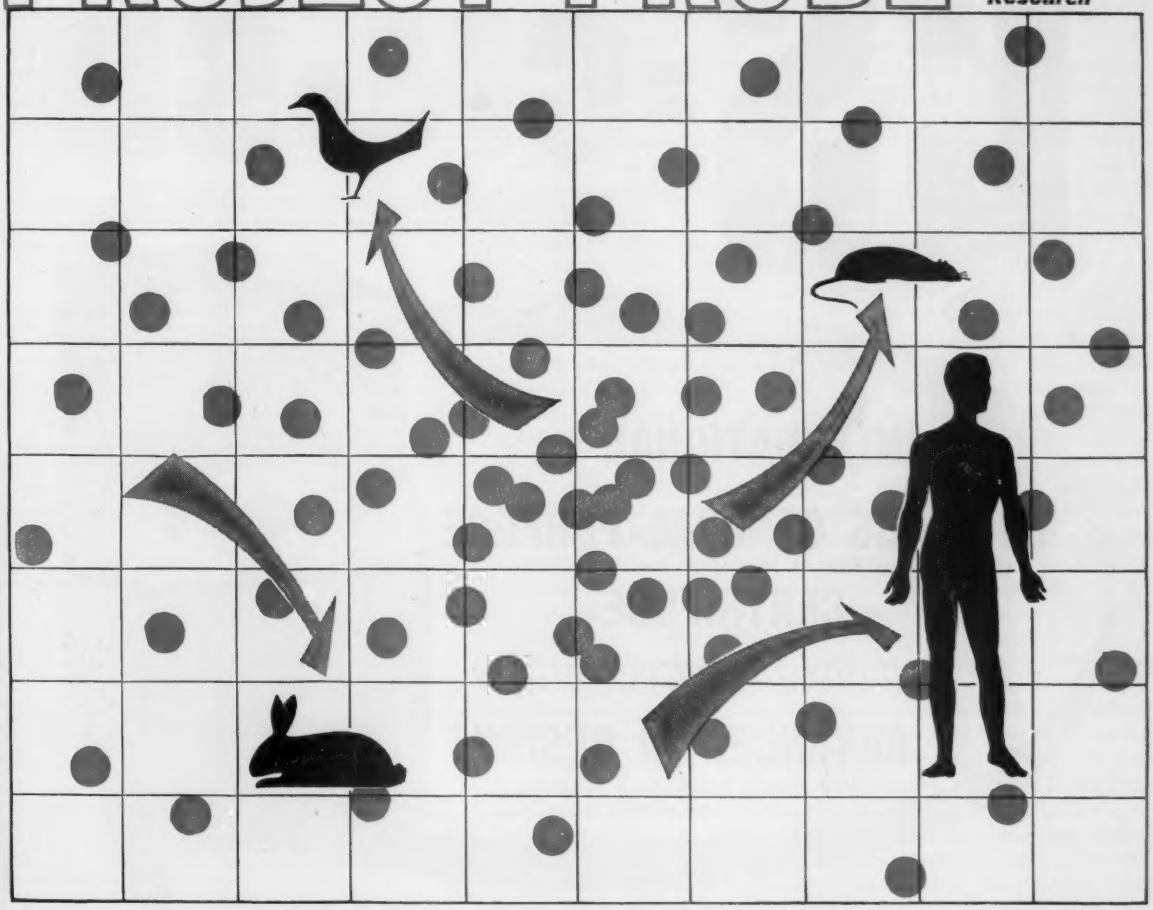
SCIENCE

Cover

Thin (200 angstroms) longitudinal section through closely packed mitochondria from the inner segment of a retinal rod, showing the characteristic arrangement of the constitutuent membranes with indications of regular internal fine structure. See page 13. (Low-temperature specimen preparation, electron microscope, about × 245,000.) [Humberto Fernández-Morán, Massachusetts General Hospital]

MELPAR LAUNCHES: PROJECT PROBE

The Parade of Disciplines in the Most Advanced Areas of ***Bioscientific Research***



Today, launching a diversity of bioscientific programs, Melpar is probing many new areas in depth and breadth in all of the life sciences. Under the leadership of Dr. Milton A. Mitz, these include such areas as:

Bio-organic Chemistry, the isolation and characterization of natural products.

Physiological Chemistry, the mode action of drugs and the general problems of intermediate metabolism.

Biological Chemistry, electronic nature of nerve action.

Enzymology, the chemical structure, the kinetic mechanism, and the specific function of biological catalysts.

What is the nature of nerve action? What is the function of a biological catalyst? These represent but a few of the areas Melpar is now exploring. This is Melpar: Project Probe.

Scientists with advanced degrees in Biochemistry, who are interested in participating in **Melpar: Project Probe,** are invited to write to F. J. Drummond, Professional Placement Manager, 3348 Arlington Boulevard, Falls Church, Virginia.

MELPAR INC

A Subsidiary of Westinghouse Air Brake Company

6 January 1961, Volume 133, Number 3445

SCIENCE

SCIENCE, now combined with THE SCIENTIFIC MONTHLY, is published each Friday by the American Association for the Advancement of Science at National Publishing Company, Washington, D.C. SCIENCE is indexed in the *Reader's Guide to Periodical Literature*.

Editorial correspondence should be addressed to SCIENCE, 1515 Massachusetts Ave., NW, Washington 5, D.C. Manuscripts should be typed with double spacing and submitted in duplicate. The AAAS assumes no responsibility for the safety of manuscripts or for the opinions expressed by contributors. For detailed suggestions on the preparation of manuscripts, see *Science* **125**, 16 (4 Jan. 1957).

Advertising correspondence should be addressed to SCIENCE, Room 740, 11 West 42 St., New York 36, N.Y.

Change of address notification should be sent to 1515 Massachusetts Ave., NW, Washington 5, D.C., 4 weeks in advance. If possible, furnish an address label from a recent issue. Give both old and new addresses, including zone numbers, if any.

Annual subscriptions: $8.50; foreign postage, $1.50; Canadian postage, 75¢. Single copies, 35¢. Cable address: Advancesci, Washington.

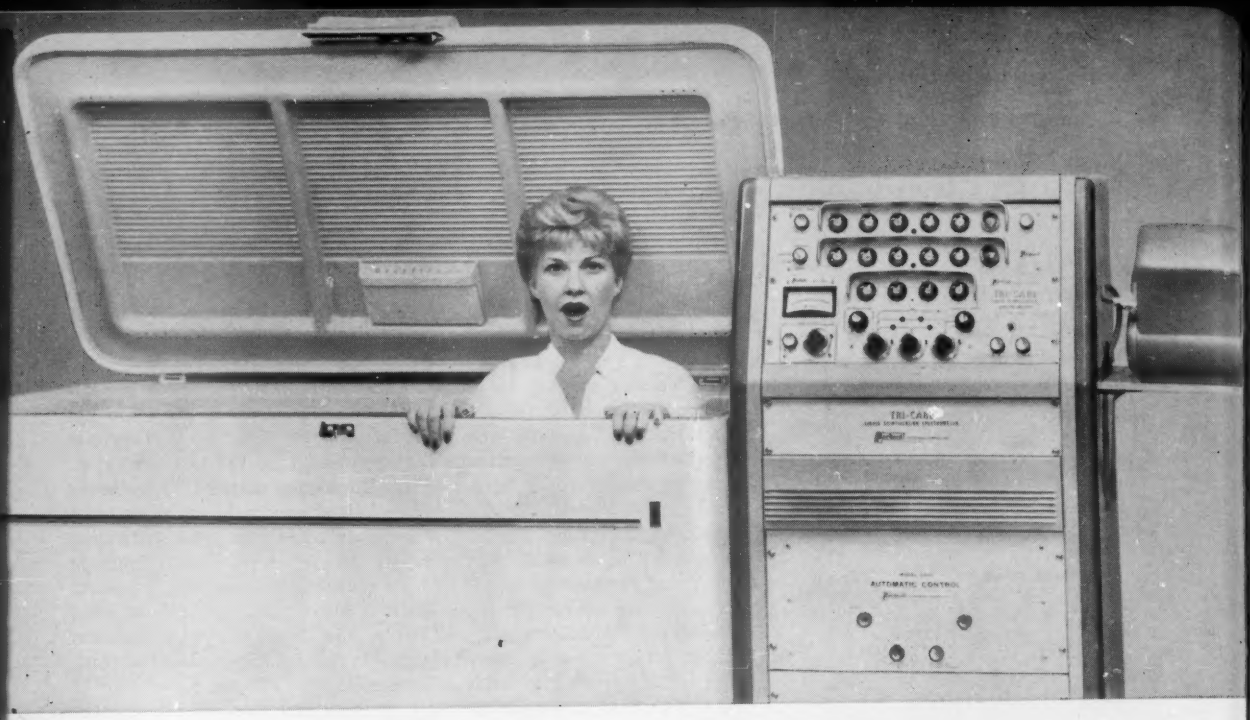
A Distinction That Needs Elaborating

A popular thesis is that a scientific belief, like "The earth is pear-shaped," may be distinguished from an ethical attitude, like "Do not steal another person's ideas," in that the belief is readily open to justification, while the attitude is not. A belief, so the argument runs, may be either true or false, with the question a matter of experiment and reason, while an attitude may be judged only right or wrong, with the question resting ultimately on private conscience. This distinction would not be so widely accepted if it were not supported by much in daily and professional life. It is also supported by a good deal of recent philosophical analysis, but such analysis also shows that without some important qualifications, the distinction can be misleading. Agreement about beliefs is not so easily achieved as the distinction would suggest, nor is the disputing of tastes as impossible.

It is easy to forget, in the glory of those moments when a scientist abandons his own beliefs to adopt those of his colleague, that new scientific ideas do not always compel instant acceptance. One obstacle to agreement over beliefs is that such agreement is not independent of common acceptance of certain attitudes. Just to hold a scientific discussion requires prior acceptance of what might be called the rules of the game. At the simplest level, this means that *A* must not only have the wit to follow *B*'s reasoning, but that *A* must be willing to listen to *B* in the first place. Some of the difficulties, for example, that have plagued the East-West talks about the technical feasibility of monitoring a nuclear test ban have been the difficulties of securing an attentive audience. The Soviets have not always been eager to listen to the scientific arguments offered by the Americans, claiming that these arguments were being offered to forestall signing a treaty.

On the other hand, in those lonely moments when we attempt to isolate and justify our most fundamental attitudes, it is easy to forget that in the ordinary course of events people often do adopt new attitudes, and that nothing can be so relevant to a change of heart as a little bit of factual knowledge. Agreement over beliefs depends, in part, on sharing attitudes, but attitudes, in turn, are a function of beliefs. In disputing attitudes, *B* may succeed in changing *A*'s attitudes by the simple expedient of correcting *A*'s beliefs. Such beliefs may range from the findings of systematic science to conclusions drawn from personal experience. It seems safe to assume, for example, that the push this country is now experiencing from segregation of the races to integration is, in part, the result of better distribution of knowledge about the qualities of the persons being discriminated against and about the consequences of discrimination to everyone concerned.

These few examples suggest that, taken without further elaboration, the popular view concerning the distinction between beliefs and attitudes can misrepresent the actual process by which men deal with one another, and so mislead us in our expectations. Perhaps we should be a little less ready to assume that when scientific experts are brought together they will iron out their differences as a matter of course, especially when the time is short and the stakes are high. Perhaps also we should be prepared to grant that attitudes are not merely matters of personal idiosyncracy, but are, in a perfectly legitimate sense, open to justification.—J.T.



It's What's Inside That Counts!

If you are counting radioactive isotopes . . .

tritium, carbon-14, iodine-131,
iron-59 or any other alpha,
beta or gamma tracer isotope . . .

you should know about the latest transistorized instruments designed and manufactured by Packard.

Auto-Gamma System

Series 250A Automatic Scaler

Whether or not you are planning to purchase new equipment, you will be interested in our latest bulletins which show "what's inside" these instruments that makes them count so well . . . so reliably.

Write or telephone requesting new instrument bulletins.

TRI-CARB LIQUID SCINTILLATION SPECTROMETERS • AUTO-GAMMA SPECTROMETER SYSTEMS
FLOW DETECTORS • SCALERS • RATEMETERS

Packard *Instrument Company, Inc.*

BOX 428 • LA GRANGE, ILLINOIS • *Phone HUnter 5-6330*

CHICAGO • ALBUQUERQUE • ATLANTA • BOSTON • LOS ANGELES • NEW YORK • PHILADELPHIA
PITTSBURGH • SAN FRANCISCO • WASHINGTON, D. C. • ZURICH • PARIS

6 January 1961, Volume 133, Number 3445 SCIENCE

CURRENT PROBLEMS IN RESEARCH

The Mitochondrion and Biochemical Machines

Mitochondria or their equivalents are the principal energy transducers in all aerobic organisms.

D. E. Green and Y. Hatefi

Living systems are capable of effecting a wide variety of energy transformations. Even the less-than-complete list of such transformations provided in Table 1 shows that nature has experimented successfully with a considerable number of transducing possibilities. These transformations or transductions of energy are accomplished by highly specialized and complex biochemical systems which can best be described as machines. There is often a reluctance on the part of biologists to speak of parts of living systems as machines because of the connotation of mechanical principles. But if a machine is looked upon merely as a structured device for converting energy from one form to another regardless of the details of mechanism, there need be no objection to the designation of biological transducing systems as machines.

Rarely is there one giant transducing machine in living systems; rather, there are assemblies of many small, identical machines arranged in parallel and in series. To the extent that our present knowledge permits any conclusions, it would appear that the mechanism of biological transducing machines has to be sought at the molecular level. That is to say, the transduction process takes place at the level of a single molecule or macromolecule. Indeed, there is now a growing body of knowledge about some of the molecules which are specialized for implementing a particular transduction (see Table 2). In a sense, biochemical machines may be looked upon as structured devices in which the transducing action of specialized molecules is facilitated or made possible. The structure is designed, as it were, for the optimum performance of the molecular transducer, and the structure has to be explained and interpreted from the standpoint of the physicochemical requirements or necessities of the transducing molecules.

Thus, the study of cellular machines is in essence topological enzymology. Function and structure are inextricably intertwined. Before the enzymology (in the sense of catalytic function) can be meaningful, there has to be an adequate and precise biochemical description of the structure of a given machine.

When we say that the transduction takes place at the level of a single molecule, it is implied that the transducing substance accepts energy in one form and transmits or stores energy in another form. For example, retinene (*1*) is photochemically transformed to a *trans*-isomer and is thus the molecular instrument for converting radiant energy to some form of chemical energy. Actomyosin (*2*) undergoes either molecular modification in size and shape or positional displacement when acted upon by adenosine triphosphate, thus serving as a molecular instrument for converting chemical energy to mechanical energy. Chlorophyll (*3*) is the molecular device for converting radiant energy into some as yet undefined form of chemical energy. Thus the operation of cellular machines must involve the integration of the performance of many hundreds or thousands of transducing molecules.

The key problems posed by biochemical machines are covered by the following questions: What are the component parts? How are they arranged? Which components are the molecular energy transducers and how do they work? In this article we try to give a bird's eye view of the state of progress in the study of one cellular machine—namely, the mitochondrion. The experience which is being gathered in the study of this machine may well be a guide to the problems and pitfalls which can attend exploration of other cellular machines.

Function of the Mitochondrial System

Aerobic cells of animals and plants contain a subcellular body of characteristic shape, size, structure, and staining properties, known as the mitochondrion (*4*) which serves as the principal generator of chemical energy in utilizable form (*5*). The corresponding particle in microorganisms (*6*) is functionally and chemically very similar to the mitochondrion, but it is generally of smaller size.

The universal function of all mitochondria or their structural equivalents in bacteria is to couple the aerobic oxidation of some substance (usually pyruvic acid) to the synthesis of adenosine triphosphate (ATP) from adenosine diphosphate (ADP) and inorganic phosphate. That is to say, these are devices for liberating chemical energy by oxidation and converting or harnessing this energy in the form of the bond energy of ATP (*7*). In general, the oxidation of pyruvic acid to CO_2 and H_2O

The authors are affiliated with the Institute for Enzyme Research of the University of Wisconsin, Madison. Dr. Green is codirector of the institute and Dr. Hatefi is an assistant professor.

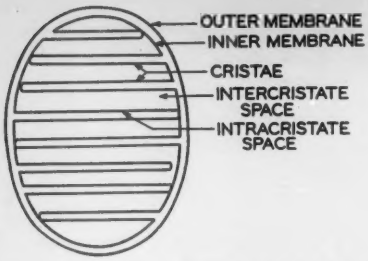


Fig. 1. Idealized structure of the mitochondrion.

by way of the citric acid cycle is the principal, if not the only, oxidative process involved. For each of the five atoms of oxygen used up in the oxidation of one molecule of pyruvic acid, three molecules of ATP are synthesized from ADP and inorganic phosphate. In other words, the complete combustion of one molecule of pyruvic acid to CO_2 and H_2O leads to the synthesis of 15 molecules of ATP (*8*).

Mitochondria can oxidize substances other than members of the citric acid cycle. Some of these substances, such as fatty acids (*9*) or amino acids (*10*) ultimately give rise to members of the citric acid cycle, while other substances, such as α-glycerophosphate (*11*) and β-hydroxybutyrate (*12*), have no direct connection at all with the citric cycle. In bacteria even inorganic substances can be oxidized by the particles concerned with terminal respiration (*13*). The universal element in all mitochondria is the coupling of oxidation to synthesis of ATP—that is, oxidative phosphorylation. The variable element can be the nature of the substances oxidized.

In addition to the basic coupling function, some, but not all, mitochondria catalyze various ATP-dependent snythetic processes, such as synthesis of phospholipid (*14*), protein (*15*), hippuric acid (*16*), and citrulline (*17*). These are secondary mitochondrial functions which apparently are not involved in the exercise of the primary coupling function.

The terminal electron transport system is one of the invariant universals of aerobic living systems. Whether isolated from heart muscle, *Azobacter*, or mung beans, its basic function is the same; it contains essentially the same catalytic components and exhibits similar, if not identical, structural patterns in all three cases. There is certainly no evidence of convergent evolution as a factor in the development of the mitochondrial system in animals, plants, and microorganisms. It would appear that once the problem of coupling electron flow to ATP synthesis had been solved in a particular fashion early in evolutionary history, no major modification in the underlying principles was introduced thereafter.

Mitochondrial Form and Structure

Mitochondria of animal and plant sources share a characteristic form and organization (*4*) (see the idealized representation in Fig. 1). The long dimension of the rod-shaped mitochondrion may be greater than 10 microns or less than 1 micron, depending upon the source. Surrounding the mitochondrion is an envelope with a double-membrane structure. Within the mitochondrion there is an array of double-membrane structures which usually are at right angles to the long axis of the particle and which may be looked upon as invaginations of the inner membrane of the envelope. These internal structures are known as cristae. External and internal membrane systems form one continuous network. The light area between the electron-dense, twin membranes of cristae and envelope probably is the locus of the internal fluid medium of the mitochondrion. If this is the case, it follows that the internal medium would bathe all the membrane structures of the mitochondrion, and furthermore, that the structured elements would interpose a mechanical barrier to the flow of solutes and solvents either from the external medium inwards or from the internal medium outwards. Thus, there are barriers within barriers which interdict the free flow of substances between the mitochondrion and the external milieu.

The mitochondria of heart muscle are packed with cristae, while those of liver contain relatively few. The greater the number of cristae per unit area, the greater the oxidative rate of the mitochondrion and the fewer are the accessory enzymatic activities—that is, activities other than or unconnected with the primary mitochondrial function. Liver mitochondria surpass all others in wealth of auxiliary functions, and this wealth is accompanied by a low density of cristae in the mitochondrion.

Sonic vibrations comminute mitochondria to much smaller particles which no longer show mitochondrial form and which represent fragments of the mitochondrial cristae and envelope

Table 1. Biological transductions.

Energy transduction	Biological transducing system
Sonic to electrical energy	Ear
Radiant to electrical energy	Eye
Mechanical to electrical energy	Skin
Chemical to electrical energy	Nerve
Radiant to chemical energy	Chloroplast
Chemical to radiant energy	Luminescing organisms (firefly)
Chemical to osmotic energy	Kidney, cell membrane
Chemical to mechanical energy	Muscle
Chemical to sonic energy	Vocal cords
Chemical to electrical energy	Electric organs in electric fish
Oxidative to utilizable chemical energy	Mitochondrion

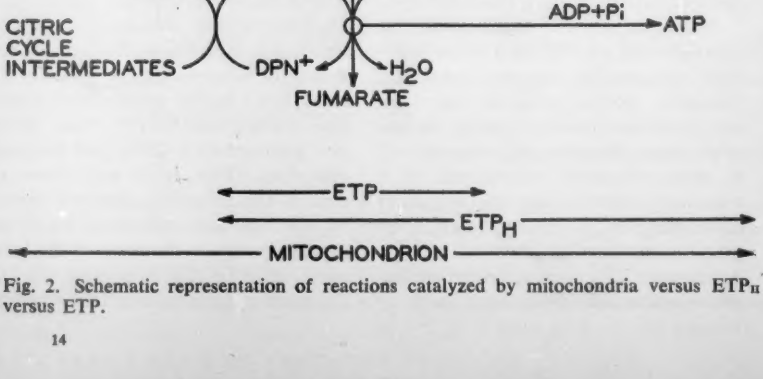


Fig. 2. Schematic representation of reactions catalyzed by mitochondria versus ETP_H versus ETP.

(*18, 19*). Some important correlations have been found between the structure of these derivative particles and the extent to which the original mitochondrial functions are preserved. Let us consider only the three basic functions: citric cycle oxidations, oxidative phosphorylation, and electron transport. As soon as mitochondrial form disappears, the capacity for implementing the complete citric cycle is lost. But as long as the derivative particle retains double membrane structure, even though mitochondrial form has been lost, the capacity for coupling oxidation to synthesis of ATP can be preserved. Finally, when the comminution produces a particle with a single membrane structure, then only the capacity for electron transport is retained. The particle with an intact electron transport chain but lacking the coupling capacity is referred to in our laboratory as the electron transport particle, or ETP (*20*), whereas the comparable particle with coupling capacity is known as ETP_H (*19*) (Fig. 2).

Thus, mitochondrial function can be eliminated or whittled down seriatim, and by similar tactics the structure of the mitochondrion can be reduced in complexity step by step. This technique of seriatim degradation and modification has proved to be the solution to the dilemma of studying a system too complex for direct analysis.

Mitochondrion as a Complete Enzymic Unit

It cannot be emphasized too strongly that the mitochondrion, when properly isolated, contains the complete repertoire of enzymes, coenzymes, and cofactors required for implementing its wide spectrum of catalytic activities (*21*). Moreover, the relative proportions of these many components are of a comparable order of magnitude and appear to be fixed. Thus, without any supplementation the mitochondrion is a complete operational unit, in which all the component parts in the proper proportions are fitted together.

Enzymes which are localized outside the mitochondrion are not found in the mitochondrion. That is to say, only enzymes pertinent to the exercise of mitochondrial function are present in any significant amount in the mitochondrion. There is thus no encouragement for the idea that the mitochondrion is a random, heterogeneous particle in which each of a large number of miscellaneous enzymes becomes occluded. On the contrary, the weight of evidence supports the view of the mitochondrion as a highly precise, organized mosaic of a strictly determined number of enzymes and coenzymes arranged in a repeating and invariant pattern.

Table 2. Components involved in biological transductions.

Component	Transducing system
Retinene 1 and 2	Eye (retina)
Rod opsin	Eye
Cone opsin	Eye
Chlorophyll	Chloroplast
Cytochrome *f*	Chloroplast
Cytochromes	Mitochondria
Coenzyme Q	Mitochondria
Flavin	Mitochondria
DPN	Mitochondria
Myosin	Muscle
Actomyosin	Muscle
ATP	Muscle
Luciferin	Firefly (*Photinus pyralis*)
Luciferase	Firefly
ATP	Firefly

Unit of Mitochondrial Function

Let us consider only one parameter of mitochondrial function—the electron transport chain, or at least that segment thereof which includes all the catalysts between reduced diphosphopyridine nucleotide (DPNH) or succinate at one end and oxygen at the other end. What is the smallest common denominator for the exercise of electron transport?

The mitochondrion, or at least the structured portion thereof, may be looked upon as a polymer of several thousand monomeric repeating units each of which contains a complete electron transport chain as defined above. In theory, then, it should be possible to comminute the electron transport particle to a size which would accommodate only a single unit. Sonic fragmentation of ETP leads to the formation of particles of very small dimensions. This may be a strong indication for the existence of such units. On the other hand, the smallest unit that can couple electron transport to the synthesis of ATP is more complex than the unit which is limited to the exercise only of the electron transport function. The minimal requirement for a particle to exercise the coupling function appears to be double membrane structure.

We may interpret this in the following way. Coupling requires a group of enzymes and factors other than those of the electron transport chain. To conserve these auxiliary enzymes, or perhaps to facilitate their action, it is necessary to have, in effect, a tube with the two ends sealed off to prevent excessive leakage out of the loosely held components in the interior. According to this interpretation, the unit for coupling is merely the unit for electron transport supplemented with a group of easily detachable factors. The double-membrane arrangement may just ensure this close association of the particulate electron transport unit with the complex of enzymes and factors essential for the coupling process.

In the same way, the loss of the capacity for citric cycle oxidations which attends the comminution of mitochondria may be a consequence merely of damage to the cristae and the subsequent leaching out of enzymes and cofactors from the interior of the cristae. In fact, when supplemented with the appropriate enzymes, ETP or ETP_H can carry out the complete citric cycle.

Thus, we may think of the electron transport chain as the ultimate unit. When separated from the milieu of the crista, it is restricted to the electron transport process. When supplemented with some of the cofactors and enzymes, it can couple electron flow to synthesis of ATP, as in ETP_H, and when supplemented with all the enzymes and cofactors, it can couple the oxidations of the citric cycle to synthesis of ATP, as in the mitochondrion.

Strategy for Study of Mitochondrial Function

By virtue of the complexity (both structural and functional) of the mitochondrion, observations of a gross character cannot penetrate very deeply its underlying chemical and physical principles. The strategy has been to trim down the mitochondrion to a point where the complexity is more manageable (*22*). In practice this has meant that the starting point for structural and functional studies has been not the mitochondrion but the less complex particle, ETP. Two of the three main facets of mitochondrial function—namely, citric cycle oxidations and the coupling of electron flow to synthesis of ATP—have been set aside, and experimental emphasis has been placed on the elucidation of the electron transport chain. Without a precise knowledge of the electron transport chain it would be difficult to decipher the principles underlying

Table 3. Components of the electron transport system.

Component	Minimal molecular weight	Absorption bands ($m\mu$)	Prosthetic group
f_S	~230,000	450 (oxidized)	Flavin dinucleotide of unknown structure
f_D	~70,000	450 (oxidized)	Flavinadenine dinucleotide
Coenzyme Q	863.4	405, 275 (oxidized in ethanol), 290 (reduced)	
Cytochrome *a*	~110,000	444, 517, 605, 835* (reduced)	*a* heme
Cytochrome *b*	~30,000	429, 530, 562 (reduced)	*b* heme
Cytochrome c_1	~38,000	418, 540, 554 (reduced)	c_1 heme
Cytochrome *c*	12,000	415, 521, 550 (reduced)	*c* heme

* Present only in the oxidized enzyme.

coupling. Once the chain is defined, the road will be clear to achieve this objective.

There is the obvious danger that when the electron transport process is no longer coupled to synthesis of ATP it may not faithfully represent the counterpart process which operates in a coupled system. This possibility has been examined, and it appears that the same electron transport process operates whether coupling takes place or not, in the sense that the sequence of components and the nature of the oxidoreductions are the same. Certain oxidoreductions can take place either with or without phosphate esterification, but there does not seem to be an essential qualitative difference between coupled and uncoupled electron transport processes (*23*).

Sequence of Components in the Chain

The electron transport particle (ETP) catalyzes the oxidation of succinate to fumarate and of DPNH to DPN^+ by molecular oxygen. Involved in these oxidations are two flavoprotein dehydrogenases (*24*, *25*), four cytochromes (*26–28*), iron (*29*) (in a form other than that of porphyrin-bound iron), copper (*29*, *30*), and a benzoquinone derivative known as coenzyme Q (*31*, *32*).

Electrons originating from either succinate or DPNH are transferred eventually to oxygen through a chain involving the cytochromes, coenzyme Q, nonheme iron, and copper. Our present state of knowledge about the sequence of components in the chain is summarized in Fig. 3. Although the idea of a single chain from coenzyme Q to oxygen is more generally accepted, several pieces of information are more consistent with the concept of two interconnecting chains, one for succinic flavoprotein dehydrogenase (f_S) and one for DPNH flavoprotein dehydrogenase (f_D). The bracket in the figure is used to indicate this possibility. Like coenzyme Q, cytochrome *b* is situated between the flavoproteins and cytochrome c_1. However, its position relative to coenzyme Q is not clear (*33*).

Components of the Electron Transport Chain

The two flavoprotein dehydrogenases (succinic and DPNH dehydrogenase) as well as the four cytochromes are proteins which have now been isolated in homogeneous state and defined with respect to molecular weight, spectrum, prosthetic group, and gross composition (see Table 3). Coenzyme Q is not found in close association with any of the six proteins and can be readily extracted and isolated as a crystalline product of molecular weight 863.4 (*32*, *34*).

The succinic dehydrogenase (f_S) (*24*) and DPNH dehydrogenase (f_D) (*25*) are both flavoprotein enzymes. The flavin prosthetic group of f_D is flavinadenine dinucleotide, while that of f_S is a dinucleotide as yet uncharacterized. The flavin group is readily split off by acid from the protein of f_D but not from the protein of f_S, and this difference in behavior is the basis of the method for estimating the proportion of f_S and f_D in a mixture. According to Kearney (*35*), the flavin prosthetic group of f_S is linked to the protein by a peptide bond which can be ruptured by proteolytic enzymes. Nonheme iron appears to be closely associated with both f_S and f_D in the ratio of at least four atoms of iron per molecule of flavin.

The four cytochromes are hemoproteins which differ in respect to both the protein and heme moieties. The heme group of cytochrome *b* (*36*) is protohemin, while that of cytochrome *a* is a heme derivable from protohemin by replacement of three of the ring substituents with a formyl group and two long-chain carbon residues (*37*). The heme group of cytochromes *c* and c_1 is also protohemin, but the heme group of cytochrome *c* (and probably that of cytochrome c_1) is attached to cysteine residues in the apoprotein by thiol ether links (*36*). The heme groups of cytochromes *a* and *b* are readily extracted from the respective apoproteins by acid acetone, whereas the link of the heme groups of cytochromes *c* and c_1 to the apoproteins is unaffected by this reagent.

Cytochrome *b* exists in two forms; one of these forms occurs in close association with succinic dehydrogenase (*38*) while the other can be isolated as a discrete protein with no functional group other than the heme (*28*). The succinic dehydrogenase has been isolated by Ziegler and Doeg (*39*) as a soluble complex containing one molecule of *b* heme per molecule of flavin, and also lipid in the amount of 18 percent by weight. At present, it is not certain whether the same protein moiety is the bearer of all three functional groups (the flavin, nonheme iron, and heme) or whether the succinic dehydrogenase as isolated is a complex of two or more proteins each with a separate prosthetic group, as has been found to be the case for the component

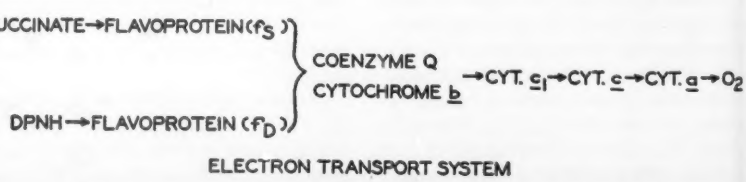
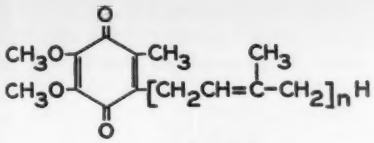


Fig. 3. Sequence of components in the electron transport system.



	SOURCE
n=10	BEEF HEART
n=9	RAT, TORULA
n=8	AZOTOBACTER
n=7	TORULA
n=6	SACCHAROMYCES CEREVESIAE

Fig. 4. Structure of coenzymes Q.

proteins of the pyruvic (*40*, *41*) and α-ketoglutaric dehydrogenase (*41*, *42*) complexes.

Cytochromes *a* and *b* are isolated as water-insoluble, polymeric particulates. These can be solubilized in water with bile salts and depolymerized to monomers by reagents such as thioglycollate (*43*) and cetyldimethylethyl ammonium bromide (*28*). Cytochromes *c* and c_1 are water-soluble as isolated, but c_1 occurs in polymeric forms (aggregates of six or more molecules) which can be depolymerized to the monomer by reagents such as thioglycollate (*27*, *44*). Cytochromes *a* and c_1, as isolated at the highest purity level, contain lipid (*27*, *45*) (about 26 and 10 percent, respectively), whereas *b* and *c* can be isolated in lipid-free forms. However, cytochrome *c* can also be shown to exist in the particle in close association with lipid (*46*).

Cytochrome *a* is isolated in the form of a hemoprotein which contains copper (*47*, *48*), the molecular ratio of copper to heme being 1:1 (*45*, *48*). This hemoprotein-copper complex catalyzes the oxidation of reduced cytochrome *c* by molecular oxygen (*45*, *49*, *50*).

Coenzyme Q is a tetrasubstituted benzoquinone with a side chain containing ten isoprenoid units (see Fig. 4) (*32*, *51*). Animal tissues generally contain coenzyme Q_{10}—that is, the coenzyme with a side chain containing ten isoprenoid units—though Q_9 has recently turned out to be the preferred homologue in the tissues of the rat (*52*). In microorganisms, coenzymes Q_6, Q_7, Q_8, Q_9, and Q_{10} have been found to occur under physiological conditions (*32*, *53*). Coenzyme Q is water-insoluble and is probably solvated in areas of high lipid concentration in the mitochondrion.

Stepwise Fragmentation of the Chain

The sequence of components in the electron transport chain has been deduced from the information obtained by fragmenting the chain into smaller units and determining the composition and the catalytic activity of the derivative segments (see Table 4).

The fragments derived by the cleavage of the mitochondrion or ETP are usually particles, though some of the simple and uncomplicated. The diffiseparation of mixtures of particles which a priori might have been expected to pose a very difficult technical problem has proved to be relatively simple and uncomplicated. The difficulty has been predominantly that of finding the reagent and the conditions which would permit the selective fragmentation of one specific bond. Once this has been achieved, the separation of particles by ultracentrifugation and salt precipitation has been straightforward.

The few reagents which have been found to be efficacious for rupturing the bonds which hold together the components of the chain (see Table 5) are soluble in both water and lipid.

Lipid in Relation to Mitochondrial Structure and Function

Lipid accounts for about 30 percent of the total dry weight of the mitochondrion and of ETP. Recent studies of Fleischer and Klouwen indicate that the composition of the lipid, regardless of the segment of the chain with which it is associated, varies little if at all (*54*). Phospholipid (*55*) accounts for the bulk of the lipid (> 90 percent). In addition to coenzyme Q, vitamin E (*56*), carotenoids (*57*), and substantial amounts of cholesterol (*55*) are found in the neutral lipid fraction. The mitochondrial lipids are characterized by fatty acid residues with a high degree of unsaturation (*55*, *58*, *59*) and by an unusually high proportion of plasmalogen (*55*, *59*).

Mitochondrial lipid readily assumes, and probably exists, in a state of orientation which, in effect, makes the lipid "soluble" in water (*60*). This property may be attributed to the phospholipid molecules which constitute the bulk of the mitochondrial lipids. While the role of lipid (except coenzyme Q) in electron transport is far from clear, the close association of lipid with most of the protein components of the chain and its activating effect in some of the catalytic functions of these components (*50*, *61*) are significant indications for the participation of lipid in electron transport and oxidative phosphorylation.

Table 4. Subfractions of ETP. In addition, cytochromes *b*, *c*, and c_1 and coenzyme Q have been isolated in pure form. Fe, nonheme iron; Q, coenzyme Q; cyt., cytochrome.

Enzymic activity of subfraction	Components
Succinic dehydrogenase	f_S, Fe
DPNH dehydrogenase	f_D, Fe
Succinic-coenzyme Q reductase	f_S, Fe, cyt. *b*
Succinic-cytochrome *c* reductase	f_S, Fe, Q, cyt. *b*, cyt. c_1
DPNH-cytochrome *c* reductase	f_D, Fe, Q, cyt. *b*, cyt. c_1
Coenzyme Q oxidase	cyt. c_1, cyt. *c*, cyt. *a*, Cu
Cytochrome *c* oxidase	cyt. *a*, Cu

Mechanism of Electron Flow

Electron flow in the mitochondrion or in ETP is an extremely rapid process. Recent studies in our laboratory indicate, for example, that a DPNH oxidase system can be reconstructed from three purified segments [DPNH-cytochrome *c* reductase (*62*), cytochrome *c*, and cytochrome oxidase] and that this system is capable of catalyzing the oxidation of DPNH with a Q_{O_2} of more than 20,000 (20,000 microliters of O_2 per hour per milligram of protein at 38°C).

This rapid flow of electrons does not seem to be the result of simple molecular collision between the components of the electron transport system. The somewhat rigid structure of the electron transport chain does not allow free movement of the electron carriers. The components with larger size, such as the flavoproteins and the cytochromes, seem to be fixed in place and capable of only restricted movement (cytochrome *c*, which is a hemoprotein of relatively small molecular weight, may be an exception). Other components,

Table 5. Fragmenting reagents.

Cholate	Thioglycollate	Ethanol
Deoxycholate	*t*-Amyl alcohol	Cetyldimethylethyl ammonium bromide
Duponol	*n*-Butanol	Triton Tweens

such as coenzyme Q, nonheme iron, and copper, which have smaller dimensions, facilitate electron transfer between the less mobile carriers.

The sum of the protein contributions by succinic dehydrogenase, DPNH dehydrogenase, and the four cytochromes, as calculated from the purified form of each, represents no more than 25 percent of the total protein of ETP. This is also true for many of the subfractions of ETP. In other words, about 75 percent or more of the protein of ETP cannot be accounted for. Perhaps this excess protein serves a multitude of functions in the mitochondrion which we are as yet unaware of. But it seems that an additional, if not the principal, function of this excess protein is to provide a framework, as it were, for the spatial arrangement of the electron transport components. We may conceive of the electron transport chain as imbedded in a matrix of "framework" proteins and lipid, and the structural arrangement of the unit of the electron transport chain is thus an expression of the close interdigitation of the "framework" proteins with the oxidation-reduction proteins.

It may well be that such an arrangement is common to transducing systems other than the mitochondrion, and the remarkable similarity of the underlying structure of transducing systems suggests that the design of a "framework" protein-lipid continuum has broad applicability (*62a*).

Oxidative Phosphorylation

Reduced to the most elementary considerations, oxidative phosphorylation may be looked upon as a consequence of three principal reactions, shown in Fig. 5. The first reaction is the passage of electrons from a reduced carrier of lower oxidation-reduction potential to an oxidized carrier of higher potential. This process involves a negative free-energy change, which is utilized in converting inorganic phosphate to a so-called "high-energy" organic phosphate (reaction 2). In the third reaction, the "high-energy" phosphoryl group (~P) is transferred to adenosine diphosphate, resulting in the formation of adenosine triphosphate.

The span in the oxidation-reduction potential ($\Delta E_0'$ at *p*H 7.0 and 25°C) between DPNH and oxygen is about 1.12 volts and between succinate and oxygen, about 0.8 volt. These values

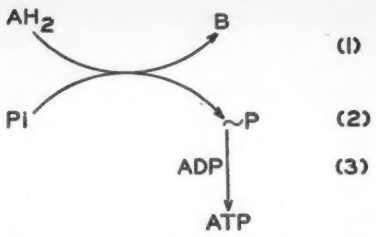


Fig. 5. Schematic representation of principal reactions in oxidative phosphorylation.

for ΔE correspond to $-\Delta F$ values of about 52,000 and 37,000 calories, respectively. In round numbers, we may say that the synthesis of 1 mole of ATP from ADP and inorganic phosphate requires 12,000 calories (*62b*). Since the oxidation of 1 mole of DPNH by oxygen is accompanied by the esterification of 3 moles of inorganic phosphate, only about 69 percent of the total free energy change involved in the oxidation is recovered in the form of the bond energy of ATP. The oxidation of succinate by oxygen shows a P/O ratio of 2, which would correspond to about 65 percent efficiency of conversion of oxidation energy to phosphate bond energy.

The experiments of Loomis and Lipmann (*63*), Copenhaver and Lardy (*64*), Nielsen and Lehninger (*65*), Slater (*66*), and Maley and Lardy (*67*), as well as those of Chance and Williams (*68*) and Chance *et al.* (*69*), have shown that the phosphorylation occurs in three separate segments of the electron transport chain. These segments are responsible for the following oxido-reductions:

DPNH ⟶ flavoprotein
flavoprotein ⟶ cytochrome *c*
and cytochrome *c* ⟶ oxygen

Since these early studies were carried out, a new member of the chain—namely, coenzyme Q—has been discovered. With a better knowledge of the components involved between flavoprotein and cytochrome *c*, it may now be possible to define more accurately the segment concerned with the second phosphorylation.

Oxidative phosphorylation as a physiological mechanism for the recovery of useful energy was first realized by Kalckar in 1937 (*70*) (see also *71*). It may seem to have taken too long to get where we are today in our understanding of the mechanism of electron transport and oxidative phosphorylation. Admittedly, we do not know all the answers yet, but we know most of the questions that remain to be answered, and we can ask them in great detail (*72*).

References and Notes

1. G. Wald and R. Hubbard in *The Enzymes*, P. D. Boyer, H. Lardy, K. Myrbäck, Eds. (Academic Press, New York, 1960), vol. 3, pt. B, p. 369.
2. A. Szent-Györgyi, *Chemistry of Muscular Contraction* (Academic Press, New York, 1951); J. Hanson and H. E. Huxley, *Symposia Soc. Exptl. Biol.* **9**, 228 (1955); M. F. Morales and J. Botts, *Arch. Biochem. Biophys.* **37**, 283 (1952); M. F. Morales in *Enzymes: Units of Biological Structure and Function* (Academic Press, New York, 1956), p. 325.
3. H. Gaffron, A. H. Brown, C. S. French, R. Livingston, E. I. Rabinowitch, B. L. Strehler, N. E. Tolbert, Eds. *Research in Photosynthesis* (Interscience, New York, 1957); D. I. Arnon, *Science* **122**, 9 (1955); M. Calvin, *Revs. Modern Phys.* **31**, 147 (1959).
4. G. E. Palade, *Anat. Record* **114**, 427 (1952); *J. Histochem. and Cytochem.* **1**, 188 (1953); in *Enzymes: Units of Biological Structure and Function* (Academic Press, New York, 1956), p. 185; F. S. Sjöstrand in *Fine Structure of Cells: Symposium, Eighth Congress on Cellular Biology, Leyden, 1954* (Interscience, New York, 1955), pp. 16, 222; F. S. Sjöstrand, *Revs. Modern Phys.* **31**, 301 (1959).
5. L. Ernster and O. Lindberg, *Ann. Rev. Physiol.* **20**, 13 (1958); O. Lindberg and L. Ernster, *The Chemistry and Physiology of Mitochondria and Microsomes* (Springer, Vienna, Austria, 1954).
6. S. Mudd, L. C. Winterscheid, E. D. Delamater, H. J. Henderson, *J. Bacteriol.* **62**, 459 (1951); S. Mudd, A. F. Brodie, L. C. Winterscheid, P. E. Hartman, E. H. Buetner, R. A. McLean, *ibid.* **62**, 729 (1951).
7. No distinction is being made between biological transducers which convert energy from one type to another and transducers which convert chemical energy from one type to another.
8. S. Ochoa, *J. Biol. Chem.* **151**, 493 (194
9. A. L. Grafflin and D. E. Green, *ibid.* 1
(1948); W. C. Schneider and V. R. Potter, *ibid.* **177**, 893 (1949); A. L. Lehninger and E. P. Kennedy, *ibid.* **179**, 957 (1949).
10. J. V. Taggart and R. B. Krakaur, *ibid.* **177**, 641 (1949); J. L. Still, M. V. Buell, D. E. Green, *Arch. Biochem.* **26**, 406 (1950); ———, *ibid.* **26**, 413 (1950).
11. R. L. Ringler and T. P. Singer, *J. Biol. Chem.* **234**, 2211 (1959).
12. D. E. Green, J. G. Dewan, L. F. Leloir, *Biochem. J.* **31**, 934 (1937); A. L. Lehninger, H. C. Sudduth, J. B. Wise, *J. Biol. Chem.* **235**, 2450 (1960).
13. S. Taniguchi, R. Sato, F. Egami, in *Inorganic Nitrogen Metabolism*, W. D. McElroy and B. Glass, Eds., (Johns Hopkins Press, Baltimore, 1956), p. 87; M. Ishimoto, J. Koyama, Y. Nagai, *J. Biochem. (Tokyo)* **41**, 763 (1954).
14. E. P. Kennedy, *J. Am. Chem. Soc.* **75**, 249 (1953); ——— and H. M. Bergoff, *J. Biol. Chem.* **201**, 393 (1953).
15. H. M. Bates, V. M. Craddock, M. V. Simpson, *J. Biol. Chem.* **235**, 140 (1960).
16. P. P. Cohen and R. W. McGilvery, *ibid.* **166**, 261 (1946); N. K. Sarkar, H. Beinert, M. Fuld, D. E. Green, *Arch. Biochem.* **37**, 140 (1952).
17. P. P. Cohen and M. Hayano, *J. Biol. Chem.* **170**, 687 (1947).
18. W. McMurry, G. F. Maley, H. Lardy, *Ibid.* **230**, 219 (1958); W. W. Kielley and J. R. Bronk, *ibid.* **230**, 521 (1958); D. M. Ziegler, A. W. Linnane, D. E. Green, M. S. Dass, H. Ris, *Biochim. et Biophys. Acta* **28**, 524 (1958).
19. A. W. Linnane and D. M. Ziegler, *Biochim. et Biophys. Acta* **29**, 630 (1958).
20. F. L. Crane, J. L. Glenn, D. E. Green, *ibid.* **22**, 475 (1956).
21. D. E. Green, *Biol. Revs. Cambridge Phil. Soc.* **26**, 410 (1951); ——— and J. Järnfelt, *Perspectives in Biol. and Med.* **2**, 163 (1959).
22. D. E. Green, *Harvey Lectures, Ser. 52 (1956-57)* (1958), p. 177.
23. A. W. Linnane and E. B. Titchner, *Biochim. et Biophys. Acta* **39**, 469 (1960).

24. T. P. Singer and E. B. Kearney in *Methods of Biochemical Analysis*, D. Glick, Ed. (Interscience, New York, 1957), vol. 4, p. 312.
25. B. De Bernard, *Biochim. et Biophys. Acta* **23**, 510 (1957); D. M. Ziegler, D. E. Green, K. A. Doeg, *J. Biol. Chem.* **234**, 1916 (1959).
26. D. Keilin and E. F. Hartree, *Nature* **176**, 200 (1955); E. Yakushiji and K. Okunuki, *Proc. Imp. Acad. (Tokyo)* **16**, 299 (1940); ———, *ibid.* **27**, 263 (1941); D. Keilin, *Proc. Roy. Soc. (London)* **98B**, 312 (1925); I. Sekuzu and K. Okunuki, *J. Biochem. (Tokyo)* **43**, 107 (1956).
27. D. E. Green, J. Järnefelt, H. D. Tisdale, *Biochim. et Biophys. Acta* **31**, 34 (1959); *ibid.* **38**, 160 (1960).
28. R. Bomstein, R. Goldberger, H. Tisdale, *Biochem. Biophys. Research Comm.* **2**, 234 (1960).
29. D. E. Green in *Enzymes: Units of Biological Structure and Function* (Academic Press, New York, 1956), p. 465; F. L. Crane, J. L. Glenn, D. E. Green, *Biochim. et Biophys. Acta* **22**, 475 (1956).
30. B. Eichel, W. W. Wanio, P. Person, S. J. Cooperstein, *J. Biol. Chem.* **183**, 89 (1950).
31. F. L. Crane, Y. Hatefi, R. L. Lester, C. Widmer, *Biochim. et Biophys. Acta*, **25**, 220 (1957); Y. Hatefi, R. L. Lester, F. L. Crane, C. Widmer, *ibid.* **31**, 490 (1959); R. A. Morton, *Nature* **182**, 1764 (1958).
32. R. L. Lester, Y. Hatefi, C. Widmer, F. L. Crane, *Biochim. et Biophys. Acta* **33**, 169 (1959).
33. Y. Hatefi, P. Jurtshuk, A. G. Haavik, in preparation.
34. F. L. Crane, R. L. Lester, C. Widmer, Y. Hatefi, *Biochim. et Biophys. Acta* **32**, 73 (1959).
35. E. B. Kearney, *J. Biol. Chem.* **235**, 865 (1960).
36. K. G. Paul in *The Enzymes*, P. D. Boyer, H. Lardy, K. Myrbäck, Eds. (Academic Press, New York, 1960), vol. 3, pt. B, p. 277.
37. M. Morrison, J. Connelly, J. Petix, E. Stotz, *J. Biol. Chem.* **235**, 1202 (1960).
38. K. A. Doeg, S. Krueger, D. M. Ziegler, *Biochim. et Biophys. Acta* **41**, 491 (1960).
39. D. M. Ziegler and K. A. Doeg, *Biochem. Biophys. Research Comm.* **1**, 344 (1959).
40. V. Jagannathan and R. S. Schweet, *J. Biol. Chem.* **196**, 551 (1952); R. S. Schweet, B. Katchman, R. M. Bock, V. Jagannathan, *ibid.* **196**, 563 (1952).
41. I. C. Gunsalus, in *The Mechanism of Enzyme Action*, W. D. McElroy and B. Glass, Eds. (Johns Hopkins Press, Baltimore, 1954), p. 545.
42. D. R. Sanadi, J. W. Littlefield, R. M. Bock, *J. Biol. Chem.* **197**, 851 (1952); D. R. Sanadi, M. Langley, R. L. Searls, *ibid.* **234**, 178 (1959); D. R. Sanadi, M. Langley, F. White, *ibid.* **234**, 183 (1959); V. Massey, *Biochim. et Biophys. Acta* **32**, 286 (1959); M. Koike, L. J. Reed, W. R. Carroll, *J. Biol. Chem.* **235**, 1924 (1960); M. Koike and L. J. Reed, *J. Biol. Chem.* **235**, 1931 (1960); M. Koike, P. C. Shah, L. J. Reed, *ibid.* **235**, 1939 (1960).
43. K. S. Ambe and A. Venkataraman, *Biochem. Biophys. Research Comm.* **1**, 133 (1959).
44. R. S. Criddle and R. M. Bock, *ibid.* **1**, 138 (1959).
45. D. E. Griffiths and D. C. Wharton, unpublished studies.
46. C. Widmer and F. L. Crane, *Biochim. et Biophys. Acta* **27**, 203 (1958).
47. C. V. Wende and W. W. Wainio, *J. Biol. Chem.* **235**, PC11 (1960); S. Takemori, I. Sekuzu, K. Okunuki, *Biochim. et Biophys. Acta* **38**, 158 (1960).
48. R. H. Sands and H. Beinert, *Biochem. Biophys. Research Comm.* **1**, 175 (1959).
49. D. Keilin and E. F. Hartree, *Nature* **141**, 870 (1938); L. Smith and E. Stotz, *J. Biol. Chem.* **209**, 819 (1954); K. Okunuki, I. Sekuzu, T. Yonetani, S. Takemori, *J. Biochem. (Tokyo)* **45**, 847 (1958).
50. Y. Hatefi, *Biochim. et Biophys. Acta* **30**, 648 (1959).
51. R. A. Morton, G. M. Wilson, J. S. Lowe, W. M. F. Leat, *Chem. & Ind. (London)* **1957**, 1649 (1957); D. E. Wolf, C. H. Hoffman, N. R. Trenner, B. H. Arison, C. H. Shunk, B. O. Linn, J. F. McPherson, K. Folkers, *J. Am. Chem. Soc.* **80**, 4752 (1958).
52. R. E. Olson and G. H. Dialameh, *Biochem. Biophys. Research Comm.* **2**, 198 (1960); D. E. M. Lawson, E. I. Mercer, J. Glover, R. A. Morton, *Biochem. J.* **74**, 38P (1960).
53. R. L. Lester, F. L. Crane, Y. Hatefi, *J. Am. Chem. Soc.* **80**, 4751 (1958).
54. S. Fleischer and H. Klouwen, unpublished studies.
55. R. E. Basford, *Biochim. et Biophys. Acta* **33**, 195 (1959).
56. A. Nason and I. R. Lehman, *J. Biol. Chem.* **222**, 511 (1956); J. Bouman and E. C. Slater, *Biochim. et Biophys. Acta* **26**, 624 (1957).
57. F. L. Crane, R. L. Lester, C. Widmer, Y. Hatefi, *Biochim. et Biophys. Acta* **32**, 73 (1959).
58. R. T. Holman and C. Widmer, *J. Biol. Chem.* **234**, 2269 (1959).
59. E. V. Marinetti, J. Erbland, J. Kochen, E. Stotz, *ibid.* **233**, 740 (1958); G. D. Joel, M. L. Karnovsky, E. G. Ball, O. Cooper, *ibid.* **233**, 1565 (1958).
60. S. Fleischer and H. Kouwen, *Federation Proc.* **19**, 33 (1960).
61. W. W. Wainio and J. Greenlees, *Science* **128**, 87 (1958); Y. Hatefi, *Biochim. et Biophys. Acta* **34**, 183 (1959).
62. Y. Hatefi, A. G. Haavik, P. Jurtshuk, in preparation.
62a. H. Fernández-Morán, *Revs. Modern Phys.* **31**, 319 (1959).
62b. L. L. Ingraham and A. B. Pardee in *Metabolic Pathways*, D. M. Greenberg, Ed. (Academic Press, New York, 1960), vol. 1, p. 1.
63. W. F. Loomis and F. Lipmann, *J. Biol. Chem.* **179**, 503 (1949).
64. J. H. Copenhaver, Jr., and H. A. Lardy, *ibid.* **195**, 225 (1952).
65. S. O. Nielsen and A. L. Lehninger, *J. Am. Chem. Soc.* **76**, 3860 (1954).
66. E. C. Slater, *Nature* **174**, 1143 (1954).
67. G. F. Maley and H. A. Lardy, *J. Biol. Chem.* **210**, 903 (1954).
68. B. Chance and G. R. Williams, *ibid.* **217**, 383, 395, 409, 429 (1955).
69. B. Chance, G. R. Williams, W. F. Holmes, J. Higgins, *ibid.* **217**, 439 (1955).
70. H. Kalckar, *Enzymologia* **2**, 47 (1937).
71. ———, *Biochem. J.* **33**, 631 (1939); V. A. Belitzer, *Enzymologia* **6**, 1 (1939); ——— and E. T. Tsibakowa, *Biokhimiya* **4**, 516 (1939).

72. We wish to thank Dr. H. Fernández-Morán, Mixter Laboratories for Electron Microscopy, Massachusetts General Hospital, Boston, for the electron micrograph of the mitochondria of retinal rods and cones shown on the cover. For the techniques of high-resolution electron microscopy used to obtain this micrograph see H. Fernández-Morán, *J. Appl. Phys.* **30**, 2038 (1959), *Ann. N. Y. Acad. Sci.* **85**, 689 (1960). Dr. Fernández-Morán has also examined preparations of the electron transport particle (ETP) from our laboratory, and has observed a predominant type of particle 150 to 200 A in diameter with indications of substructure of the order of 15 to 20 A (private communication).

An Experiment in the History of Science

With a simple but ingenious device Galileo could obtain relatively precise time measurements.

Thomas B. Settle

On the "Third Day" of his *Discorsi* (*1*) Galileo described an experiment in which he had timed a ball accelerating along different lengths and slopes of an inclined plane. With it he believed he had established the science of naturally accelerated motion. To get a better appreciation for some of the problems he faced I have tried to reproduce the experiment essentially as Galileo described it. In the process I found that it definitely was technically feasible for him, and I think I gained a good idea of the type of results he probably looked for and of how well they turned out.

He described the experiment because, in his words: "in those sciences where mathematical demonstrations are applied to natural phenomena, as is seen in the case of perspective, astronomy, mechanics, music, and others [,] the principles, once established by well-chosen experiments, become the foundations of the entire superstructure" (*1*, p. 171). In this case his aim was to establish a science based on two principles: (i) a general definition of uniform acceleration, "such as actually occurs in nature" (*1*, p. 154), as that motion in which equal increments of velocity are added in equal times and (ii) an assumption that "the speeds acquired by one and the same body

The author is a graduate student in the history department of Cornell University, Ithaca, N.Y.

moving down planes of different inclinations are equal when the heights of these planes are equal" (*1*, p. 163). Though he could not test these assumptions directly, he claimed that he tested consequences of them which, to us, seems to carry the same weight.

This is relatively straightforward. Though Galileo did not give us a sampling of his data, he did tell us what equipment he used, and did state explicitly that his results were very good. Since we know his "principles" were correct theoretically, we should have no reason, on the face of it, to doubt any of the particulars.

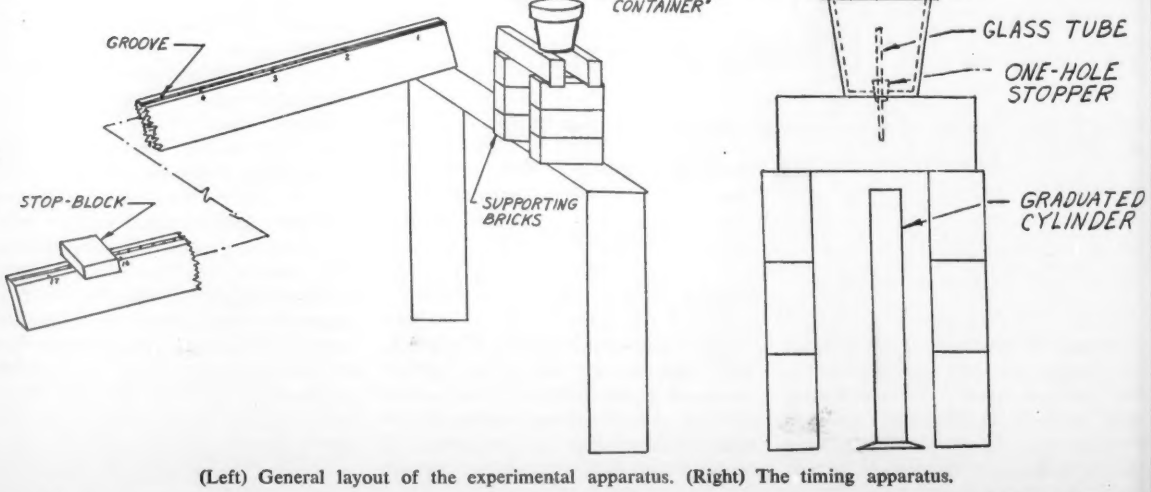
Yet they have been doubted. Before the publication of the *Discorsi*, Marin Mersenne had seen references to the experiment which lacked experimental detail. From these he had tried to perform the experiment; and because, probably, of a combination of conceptual and experimental errors, which we need not explore here, he concluded: "Ie doute que le sieur Galilee ayt fait les experiences des cheutes sur le plan, . . . l'experience n'est pas capable d'engendrer vne science" (*2*). Perhaps taking his cue from Mersenne, Alexandre Koyré has recently commented on the "amazing and pitiful poverty of experimental means at his [Galileo's] disposal": "A bronze ball rolling in a 'smooth and polished' wooden groove! A vessel of water with a small hole through which it runs out and which one collects in a small glass in order to weigh it afterwards and thus measure the times of descent (the Roman waterclock, that of Ctesebius, had been already a much better instrument): what an accumulation of sources of error and inexactitude!" (*3*).

An interesting conclusion, but I think a bit premature. To my knowledge no one has ever tried to perform an experiment equivalent to the one Galileo described. The laws of acceleration have been demonstrated many times with more sophisticated techniques; but no one, including Mersenne, has ever tried to find out if Galileo's wooden channel and water timing device actually worked, or what sort of results he accepted as the foundations of his new science. If these questions were merely of antiquarian interest we could leave them to the mercy of each individual's philosophic predisposition. But they are more; they weigh heavily upon, and are in fact basic to, any adequate evaluation of the logico-scientific status of Galileo's exposition of naturally accelerated motion, his real contributions to science, or his views on the nature of science and the need for experiment.

I hope to show that this experiment, once conceived and brought to full maturity, is simple, straightforward, and easy to execute. Thus far I can only reproduce the end product of a process of evolution (in Galileo's own mind) which may have covered 20 years. There is, in addition, a fascinating and vastly important body of knowledge concealed in the "conceiving" and "bringing to maturity" of both the theoretical and empirical aspects of this experimentation, just as in most other significant departure points in the history of experimental science. Eventually we would like to know the actual evolution of Galileo's thought in time as well as logic. For each step of original work we would like to know the mistakes and dead ends, the contributions and limitations of the existing technology and mathematics, the many conceptual aids as well as hindrances inherited from his contemporaries, and the nature and significance of his own predispositions. This could, we would hope, give us broader insights into the formative stages of any new discipline. But for now our aims are more limited.

First, let us see what Galileo himself says of the experiment (*1*, pp. 171–72):

> A piece of wooden moulding or scantling, about 12 [braccia (*4*)] long, half a [braccio] wide, and three finger-breadths thick, was taken; on its edge was cut a channel a little more than one finger in breadth; having made this groove very straight, smooth, and polished, and having lined it with parchment, also as smooth and polished as possible, we rolled along it a hard, smooth, and very round bronze ball. Having placed this board in a sloping position, by lifting one end some one or two [braccia] above the other, we rolled the ball, as I was just saying, along the channel, noting, in a manner presently to be described, the time required to make the descent. We repeated this experiment more than once in order to measure the time with an accuracy such that the deviation between two observations never exceeded one-tenth of a pulse beat. Having performed this operation and having assured ourselves of its reliability, we now



(Left) General layout of the experimental apparatus. (Right) The timing apparatus.

rolled the ball only one-quarter the length of the channel; and having measured the time of its descent, we found it precisely one-half of the former. Next we tried other distances, comparing the time for the whole length with that for the half, or with that for two-thirds, or three-fourths, or indeed for any fraction; in such experiments, repeated a full hundred times, we always found that the spaces traversed were to each other as the squares of the times, and this was true for all inclinations of the plane, i.e., of the channel, along which we rolled the ball. We observed that the times of descent, for various inclinations of the plane, bore to one another precisely that ratio which, as we shall see later, the Author had predicted and demonstrated for them.

For the measurement of time, we employed a large vessel of water placed in an elevated position; to the bottom of this vessel was soldered a pipe of small diameter giving a thin jet of water, which we collected in a small glass during the time of each descent, whether for the whole length of the channel or for a part of its length; the water thus collected was weighed, after each descent, on a very accurate balance; the differences and ratios of these weights gave us the differences and ratios of the times, and this with such accuracy that although the operation was repeated many, many times, there was no appreciable discrepancy in the results.

Then let us recognize what, exactly, Galileo sought, so that we will demand no more of his work than he did himself. Galileo thought in the language and form of Euclidean geometry. He had neither the apparatus of functional mathematics nor the interdefined system of standard weights and measures which would allow him to work with such a formula as $s = \frac{1}{2}gt^2$. He designed his equipment for less sophisticated use. In substance, he only asked it to show that: (i) for a given inclination of the plane, the distances a ball travels are in direct proportion to the squares of the time intervals (*5*):

$$S_1/S_2 = T_1^2/T_2^2 \qquad (1)$$

and (ii) for planes of different inclinations, the times of descent are proportional directly to the distance of travel and inversely to the square root of the vertical height of fall (*6*):

$$T_1/T_2 = (L_1/L_2)\ (H_2/H_1)^{\frac{1}{2}} \qquad (2)$$

This is important for at least three reasons. We must not ask him to give us a value for the acceleration due to gravity as we understand the term. Our "*g*" only came much later, after a great deal of further development in physics and mathematics (*7*). Nor should we expect him necessarily to give determinations that might be interpreted as an early form of the same thing. In addition, we see there is little justice in Koyré's criticism that Galileo failed to account for rotational inertia (*3*). Not only did the problem not exist in his mind, but it was irrelevant to the proof of his laws. The functional equivalent for

$$s = \tfrac{1}{2}gt^2$$

for a ball on an inclined plane is

$$s = \tfrac{1}{2}\ (5/7)(a/c)gt^2,$$

a/c being the ratio, for a given slope, of the vertical height of fall to the slope length. The factor 5/7 accounts for rotational inertia; being constant, it does not affect the proportionalities given above. Finally, because he could work entirely with ratios, Galileo could be completely arbitrary in his choice of measures.

Reproducing the Experiment

The most difficult part of executing the experiment lay in the necessity of choosing equipment and procedures which were available to Galileo or which were inherently no better than those he could muster. In making a plane, for instance, I assumed that he would have had excellent craftsmen at his disposal but that the work would have been done essentially by hand. Nonetheless, after choosing a 2- by 6-inch pine plank 18 feet long, with a straight grain and few knots, I had a ¼-inch rectangular groove cut in one edge with a circular saw (*8*). This done, I hand-sanded the surfaces, applied wood filler, and thoroughly rubbed in wax, making the rolling edges of the groove hard and smooth. Even so, there were irregularities where knots or the grain crossed the groove. But I made no further attempt to make the edges exactly parallel over the whole length.

I used both a standard billiard ball and a steel ball bearing, respectively about 2¼ inches and ⅞ inch in diameter.

For time measurement I used an ordinary flowerpot as a water container and threaded a small glass pipe through its bottom hole for the outflow. In all the live runs this pipe was 4½ inches long and had an inside diameter of about 0.18 inch. Its upper end was positioned high enough for me to cover it easily with a finger while my palm rested on the rim of the pot. Instead of collecting the water and then weighing it on a balance, I collected it in a graduated cylinder and "weighed" it by reading its volume in milliliters.

Then, for each reading, I placed a wooden block at a predetermined distance down the slope; filled the pot with water while holding a finger over the inside end of the pipe; filled the pipe by letting the water flow briefly; took an initial reading of the water level in the graduated cylinder; placed the ball at the starting position on the plane with my free hand; released the ball and lifted my finger simultaneously; replaced my finger at the sound of the ball striking the block; and took a final reading of the graduated cylinder.

How good was all this? From a study of the ratios we know that Galileo had to make only three measurements: slope length, vertical height of fall, and time. The first was easy; I marked off the plane in even foot lengths, using a 1-foot architect's scale. Actually, all either I or Galileo needed was a compass sufficiently large to mark off convenient unit lengths and sufficiently rigid to do it accurately. Then ratios of length turn out to be rational fractions.

Galileo did not mention how he measured vertical height, but water-level techniques for various purposes had been used in the building trades for centuries, and measuring heights would have presented no serious problem. I took a long piece of flexible tubing, fixed a short length of glass pipe in either end, and filled it with water. Placing the meniscus in one pipe at a mark near the lower end of the plane, I could measure vertically from the meniscus of the other pipe to a mark near the upper end. For each inclination we need only one such measure to compare with the distance between marks. The scales do not even have to be to the same base.

Of the three measurements, the measurement of time is the most controversial and the most difficult. With a little thought we find that it has two crucial aspects: we want the flow from the pipe to be uniform for at least the period of our longest readings, and we need to practice so that we can actually release the ball and the water flow at the same time and stop the flow at the

strike of the ball without anticipation or delay.

First, we must remember that the operator is an integral part of the apparatus. He must spend time getting the feel of the equipment, the rhythm of the experiment. He must consciously train his reactions. And each day, or at the end of each break, he must be allowed a few practice runs to get warmed up. Galileo accomplished all this by repeating the experiment "many, many times."

Table 1. Sample of experimental results and calculations which confirm Eq. 2.

Distance	Time (ml of water)		
	(Exp.)	(Av.)	(Cal.)
15	88	90+	90+
	91		
	91		
	90		
	90		
	90		
	90		
	89		
	90		
13	84	84	84
	84	base	
	84		
	84		
	84		
	84		
10	72	72+	74−
	73		
	72		
	72		
	72		
	72		
7	62	62−	62−
	61		
	62		
	61		
	62		
	62		
	62		
5	53	52	52+
	53		
	53		
	53		
	53		
	52		
	53		
	51		
	51		
	52		
	53		
	51		
3	40	40	40+
	40		
	40		
	41		
	39		
	41		
	40		
1	26		
	17		
	25		
	24		
	23		
	25		
	23	23.5	23+
	24		
	23		
	23		
	24		
	24		
	24		
	23		
	23		

Then we must remember that this is not a water clock; it is what it is and no more—a container for water with a pipe of small diameter in its bottom and with no dials, falling weights, or gear trains. All we are interested in, we find, is maintenance of a constant flow in the pipe for a maximum of 8 seconds. How can we test this? Galileo mentions a "pulse beat." Is it possible that he checked his own flow rate against a beating pendulum, a *pulsilogia?* On this hunch I made a simple pendulum out of a piece of thin wire and the billiard ball. Since a 1-meter pendulum has a beat of about 1 second, I made this pendulum somewhat less than a meter long so that it would beat at about pulse rate. By watching the shadow of the bob against vertically lined paper I could accurately lift and reset my finger in the timer at the end of a beat. I found, after collecting water at intervals of 2, 4, 6, 8, and 10 beats, that the flow was indeed constant within the limits of precision discussed below (*9*).

As a matter of interest, using the second-hand on my watch and timing for 5- and 10-second intervals, I made a rough determination of the rate of flow and found it to be 19.5 milliliters per second. It followed that, if I could measure a definite interval to within 2 milliliters, my apparatus would be precise to almost 1/10 second. In fact, it was very common to get sets of points well within this limit, to 1 milliliter or about 1/20 second. Is this better than Galileo could have done? My flowerpot was probably smaller than his "large vessel," giving me a greater fall of head for each reading. If my flow was "constant," his certainly was. Then the only thing in doubt is the "weighing." From Agricola we learn that early 16th century assayers could weigh with precision to the equivalent of 0.2 grams (*10*). My cylinder was graduated to 2 milliliters, and I read to 1 milliliter—a measurement five times as crude as the one that Galileo could have commanded.

We note further that Galileo, though presenting his results as valid for all slopes, only claimed to have successfully tested relatively shallow ones.

Table 2. Experimental data obtained with the billiard ball for the bases of three slopes, and times computed from one of the other slopes. *L*, slope length; *a*, vertical height; *T*, time.

Slope	Experimental data			Calculated data
	L	*a*	T	T
a	12	2.92	117	118− (from b)
b	13	6.25	84	85− (from c)
c	9	11.47	52	51+ (from a)

Whether this was the result of experimental insight alone or of poor results obtained at steeper inclinations we do not know. But the reasons are obvious. The theoretical results are only valid if there is no slippage between the ball and the plane and since the errors in the time readings are fixed, the accuracy decreases with the shorter intervals. So I followed Galileo's example, nor did I think it particularly worthwhile to try to find a maximum practicable slope.

Experimental Results

As I have intimated, all this turned out quite well. Table 1 gives a representative sample of some experimental results and calculations which confirm Eq. 1 above. This particular run involved the billiard ball on a slope;

$$a/c = 6.25/(8\times12) \text{ inches},$$

or about 3°44′. The distances are given in Table 1, column 1.

Column 2 gives, for each distance, the several observed times in milliliters of water. In this case all except the last set were recorded one evening, this last being recorded the following morning. Here we see the process of warming up; only after the first six readings did I begin to take the results seriously.

Column 3 merely gives the sight-averages of the good readings of column 2. They serve as specific times for the distances where these are needed in further calculations or comparisons.

Column 4 shows calculated times. Whereas Galileo struggled simultaneously with two unknowns, the validity of the laws and the worth of the equipment, I was really using known and accepted laws to determine the latter. As a result I have chosen to focus on the most ticklish part of the

work, the time measurements, by comparing the experimental and theoretical determinations. For each run I chose the sight-average time for one of the middle-to-long distances as a base. Then, using the equation

$$T_1 = (S_1/S_2)^{\frac{1}{2}} \times T_2,$$

I calculated times for the other distances. Actually, we are comparing experimental points with points on a parabola passing through one of them.

This comparison needs little comment. Even the maximum deviation, at distance 10, is less than 2 milliliters, or 1/10 second. Elsewhere, by and large, the deviations are considerably less.

The check of Eq. 2 turns out just as well. To fit my data and purposes I reduced it to

$$T_1 = [(L_1/L_2)\ (a_2/a_1)]^{\frac{1}{2}} \times T_2,$$

a being a unit measure of vertical height. Table 2, columns 1–4, shows the pertinent experimental data, obtained with the billiard ball, for the bases of three slopes. Column 5 shows times computed, as noted, from one of the other slopes.

The results of the tests made with the steel ball were just as good, but I found that they were not comparable with those made with the billiard ball. For instance, on the shallowest slope, the billiard ball made the 16-foot mark in 136 milliliters but the steel ball took 4 milliliters longer. This seemed odd; theoretically, neither the mass nor the radius should affect the acceleration. By the correct formula we can calculate that both balls should have traversed the distance in 132 milliliters. Actually, because the balls run on the two edges of the groove, their "running" circumferences are slightly less than their real ones, so they require more revolutions, and more time, to cover the same distance. A rough calculation shows that this fact probably accounts for most of the discrepancies. Had Galileo noticed similar differences between results for balls of different size, he probably would have ascribed them to frictional retardation. In any case, it appears that they would not have controverted his proportionalities.

Conclusion

I have tried to emphasize the simplicity and ease with which these results were obtained. The only extended effort put into the equipment was with respect to the plane, and then only to the limits already mentioned. And except for the effort involved in developing my own ear-hand coordination, I maintained a deliberately cavalier attitude towards the procedures and measures. For instance: the striking block and the starting position were located at the marks on the slope only by eye; the vertical height reading was not taken as finely as more time and patience would have allowed; and, I am sure, the time measure was not brought to as high a polish as a larger pot, a smaller pipe, and a finer "balance" would have made possible. But with no more precise knowledge of Galileo's tools than what can be learned in the passage cited, I wanted to give "error and inexactitude" every reasonable chance to accumulate. And yet they did not.

What of this? When I said that Galileo worked with two unknowns, I meant it only from a logical point of view. By the time both the theory and the experiment had evolved to the level implicit in the *Discorsi*, Galileo would have had sufficient confidence in the worth of each independently, irrespective of their mutual confirmation. And the fact that they coincided so nicely added one more to the list of those sciences in which mathematical demonstration is appropriate to physical phenomena. But it was not as simple then as it seems now. Science could only grow on the bones of one of the deepest prejudices of the Middle Ages, one which regarded all here below as corrupt and innately lacking the perfection, mathematical or otherwise, of the real world. At one place in Galileo's other major work, the *Dialogo*, Simplicio is made to express this opinion by saying: "In physical science there is no occasion to look for mathematical precision of evidence" (*11*). By finding this excellent approach to perfection in the physical world, Galileo took a long and important step in this early phase of experimental science.

References and Notes

1. G. Galilei, *Dialogues Concerning Two New Sciences*, H. Crew and A. de Salvio, trans. (Northwestern University, Evanston and Chicago, 1946).
2. M. Mersenne, *Harmonie Universelle: Livre Second: Des movvemens de tovtes sortes de corps* (Paris, 1636–37), p. 112. Mersenne, a Minim friar and close friend of Descartes, corresponded regularly with many of the leading figures of his day and was a physicist-mathematician in his own right. When he did the work described in *Harmonie* he had access to Galileo's published material—for instance, the *Dialogo* (see *11*)—and to circulating manuscripts, but probably not to the *Discorsi*, which was only published in 1638. Although Galileo had alluded to the experiment in several places, nowhere had he given the descriptive detail present in the *Discorsi*. We may even guess that the detail given there may have been in answer to Mersenne's criticism.
3. A. Koyré, "An Experiment in Measurement," *Proc. Am. Phil. Soc.* **97**, 224 (1953).
4. Galileo used the term *braccio*; it has been translated variously as *cubit* and *yard*, to neither of which it accurately corresponds. In the *Discorsi* (p. 16) Galileo spoke of the fact that "it was not possible, either by pump or by any other machine working on the principle of attraction, to lift water a hair's breadth above 18 braccia." If 34 feet is assumed to be the equivalent in our system, 1 braccio should be close to 22.7 inches, a figure a shade higher than that usually given.
5. See G. Galilei, *Discorsi*, pp. 167–168, theorem II, proposition II.
6. See ———, *ibid.*, p. 181, theorem V, proposition V.
7. Conceptually, the acceleration due to gravity is considerably more advanced than the distance a body falls in the first second—a measurement which several of Galileo's contemporaries did try to perform. The first fits into a functional relationship with all the attendant transformation provided by the calculus; the second can only be used in calculation involving ratios of quantities subject to the same effects. The first is regarded as a special case of universal gravitation and is quite easily seen as a function of latitude, altitude, the presence of massy formations, and so on; the second, Galileo and his contemporaries generally regarded as constant over the surface of the earth and extending, only hypothetically if at all, undiminished to such locales as the moon. Galileo had not abstracted the notions of velocity and acceleration as quantitative entities in themselves (instantaneous velocity and acceleration), notions which "fell out in the wash" with the development of the calculus. He thought of motion in terms of total distance as compared to total time, and of acceleration as the uniform increase of "motion" from one large segment to another—that is, he talked only of total distance and time and of ratios of them.
8. Galileo did not describe in detail the shape of the groove he used or how the ball (or balls) fitted into it. I assume that he rolled the ball on the edges of the groove, as I did.
9. Each time, in filling the pot, I referred the water level to a definite mark, making it somewhat lower for the short runs and slightly higher for the longer ones. I believe, though without definite proof, that this sort of compensation was not beyond the level of Galileo's capacities.
10. G. Agricola, *De Re Metallica*, translated by H. C. Hoover (Dover, New York, 1950), appendix C.
11. G. Galilei, *Dialogue Concerning the Two Chief World Systems—Ptolemaic & Copernican*, S. Drake, trans. (Univ. of California Press, Berkeley and Los Angeles, 1953), p. 230.

Science in the News

Making Science a Vital Force in Foreign Policy

Following are excerpts from an address by James R. Killian, Jr., chairman of the Corporation of the Massachusetts Institute of Technology, given at the Silver Stein Award Dinner of the M.I.T. Club of New York, 13 December 1960.

Because of the need to give penetrating and realistic attention to every aspect of foreign policy, there is justification for examining such a specialized facet of world affairs as the impact of science on foreign policy.

That this impact is great hardly needs discussion. Science and technology together are constantly creating new conditions with which foreign policy must deal. Out of technology has come the revolution in warfare imposed by nuclear weapons and ballistic missile delivery systems. Out of it have come the political, social, and economic changes induced by the growing ease and speed of communication and transportation, leaving no nation isolated. The 'revolution of rising expectations' is in large part engendered by the power of technology to improve health and living standards and the growing awareness in underdeveloped countries of this benign power. It is engendered, too, by the recent demonstrations that technology is mobile, that the sophisticated technology of the West under favorable conditions can be quickly copied by countries of less sophistication.

Finally there is the acceleration in change itself generated by science, a factor which has introduced a wholly new order of dynamics into foreign affairs. These comprehensive ways in which science and technology alter the relations among peoples must be taken into consideration if we are to shape our foreign policy wisely. . . .

Prestige and Cooperation in Space

Since World War II the status-seekers in the community of nations have relied increasingly on science and technology to build their prestige. The Soviets especially have used technology as an instrument of propaganda and power politics, as illustrated by their great and successful efforts—and careful political timing—in space exploration. They have sought constantly to present spectacular accomplishments in space technology as an index of national strength, and too often the press and the public at large have interpreted these spectacular exploits as indices of strength.

It must be admitted that spectacular accomplishments in space technology have enhanced the prestige of the Soviet Union, and we can all admire their achievements. But their expensive emphasis on space exploration will not be enough in the long pull to sustain an image of strength. This will only be accomplished by a balanced effort in science and technology. True strength and lasting prestige will come from the richness, variety, and depth of a nation's total program and from an outpouring of great discoveries and creative accomplishments on a wide front by its scientists and engineers.

These observations are by way of introduction to some of my personal views and questions regarding the U.S. space program, which so often is discussed in terms of its propaganda values and so frequently evaluated in terms of a space race with the Soviets.

I believe that in space exploration, as in all other fields that we choose to go into, we must never be content to be second best, but I do not believe that this requires us to engage in a prestige race with the Soviets. We should pursue our own objectives in space science and exploration and not let the Soviets choose them for us by our copying what they do. We should insist on a space program that is in balance with our other vital endeavors in science and technology and that does not rob them because they currently are less spectacular. In the long run we can weaken our science and technology and lower our international prestige by frantically indulging in unnecessary competition and prestige-motivated projects. So far our space program has been well planned and remarkably successful; by concentrating on scientific discovery and on such practical technological objectives as improved weather forecasting and communications, we have exploited our own special genius and proceeded in the great tradition of American science and technology.

Today, however, the pressures are very great to engage in an item-by-item race with the Soviets. Our man-in-space program is the principal victim of these pressures, and it is certain to present some difficult policy questions in the near future. It may be argued that the appeal of space exploration by man is so great that nothing will deter his engaging in manned exploration. It also may be argued that our man-in-space program is trying to proceed too fast and that it is on the way to becoming excessively extravagant and will be justified only as a competitor for world prestige with the Soviet man-in-space program. Many thoughtful citizens are convinced that the really exciting discoveries in space can be realized better by instruments than by man.

Decisions must soon be made as to how far we go with our man-in-space program and the future scale of our total space efforts. Unless decisions result in containing our development of man-in-space systems and big rocket boosters, we will soon have committed ourselves to a multibillion-dollar space program. I have never seen any public statement estimating the costs of the successive generations of big boosters for man-in-space or for the other parts of the program. How many billions of dollars will they cost over the next decade or more? How much is it likely to cost to orbit a man about the earth, to achieve a manned circumnavigation of the moon, or a lunar landing? The public should have some feel for the magnitudes involved. However much they may cost, we may decide we must spend the money, but we should make this decision with a clear understanding of the startling costs entailed. We should not permit ourselves to slide unwittingly past a point of no return or to make the commitment without comparing its desirability with alternative expenditures.

The American people must face these questions as they seek to achieve a desirable balancing of our total national effort, particularly in the use of our scientists and engineers. I do not oppose a man-in-space program. I ask that

we give the public a better opportunity to understand and to debate the rate at which we proceed. They must seek to determine whether we are now proceeding too rapidly and whether we can manage the present program without weakening other important national programs, including defense. They must face up to the tough decision as to whether we can justify billions of dollars for man-in-space when our educational system is so inadequately supported—whether our system of values assigns greater importance to this kind of exploratory activity or to the development of intellectual quality. Will several billion dollars a year additional for enhancing the quality of education not do more for the future of the United States and its position in the world than several billion dollars a year additional for man-in-space? The image of America may be shaped by the quality of its inner life more than by its exploits in outer space. . . .

Let me next discuss the great importance of voluntary international cooperation in science, and let me start by recounting a specific policy question that came before our Department of State two years ago. Should the United States support a United Nations space research program?

Despite their advocacy of international cooperation in space research, many informed American scientists felt it would be undesirable for the United Nations Committee on the Peaceful Uses of Outer Space to undertake space research and exploration, and they strongly urged that we not support a charter for the committee that would call for this kind of operational responsibility at this time. They were led to this position by the great success of the International Geophysical Year, which was conducted not by a political body such as the United Nations, but by a private, nonpolitical, nongovernment organization, the International Congress of Scientific Unions. The conviction was strongly held that international cooperation in space research and exploration could best be encouraged and coordinated by the Space Committee (COSPAR) of this volunteer private federation. This position prevailed in the United Nations, and its Committee on the Peaceful Uses of Outer Space was limited in its responsibility to the study of the regulatory and legal aspects of space, the exchange and dissemination of information on outer space, and the encouragement of space science.

So far this seems to have been a wise position. COSPAR does not have to face political issues and as a result, its scientist members, including the representatives of the Soviet Union, have come together in the context of a true scientific conference to reach agreements—without much more display of differences than can be expected in international scientific meetings.

Political scientists may well question—and some have—the desirability of thus by-passing an international political organization in furthering international cooperation. Is it not going to be ultimately necessary, they ask, to learn how to make the political organization effective in such matters? This is a legitimate question, but this case history of the Committee on the Peaceful Uses of Outer Space is illustrative of the impact of scientific views and experience on foreign affairs, and so far the scientists are supported by the unmistakable evidence that international groups of scientists seem able to achieve cooperation of great importance when they are free of political entanglements and can act freely with the tropism toward cooperation which is traditional among scientists. So far the U.N. Committee has been boycotted by the Soviets, who have raised questions of parity in East-West membership and who have insisted on a Russian being chairman. We have urged a chairman from a neutral country. Proposals are now under consideration in the United Nations for an international conference on the peaceful uses of outer space. In my judgment such a conference is greatly to be desired.

Factors in Foreign Policy

Let me present an eleven-point program for enhancing the contributions of science and engineering to the formulation of sound foreign policy and to Free World strength.

1) Recognize and stress the contributions which science can make to peace and encourage scientific activities abroad—as, for example, the betterment of health, the improvement of agriculture, and basic research—which are manifestly peaceful and benign.

2) Encourage more of the IGY type of programs which are managed by nonpolitical, private scientific organizations.

3) Encourage more international conferences such as the Conference on the Peaceful Uses of Atomic Energy. Specifically support the proposed U.N. conferences on the peaceful uses of outer space and on technical aid.

4) Despite aggravations and difficulties, continue to encourage exchange of scientific personnel between East and West. Reduce petty restrictions on scientists invited to the United States.

5) Undertake periodically a thorough review of our technical aid policies and programs to insure that they are well adapted to the countries they are intended to help. Seek the advice of knowledgeable scientists and engineers in conducting these reviews and strive for programs which bring the benefits of science in all its phases to less-favored countries.

6) Provide in Washington a mechanism for coordinating research programs and other scientific activities which government agencies sponsor abroad and make sure that our ambassadors have the opportunity, in each country where such work is conducted, to coordinate it locally.

7) Widen the role of the science adviser to the Secretary of State and continue to build strength in the corps of science attachés. Give this science adviser a role to play in strengthening the competence of the State Department to deal with the technical aspects of arms limitation. Support the continuation of NATO's science advisory services.

8) Encourage regional programs to strengthen science not only in Europe but in other parts of the world. Science lends itself well to international efforts. CERN is an example.

9) Encourage international efforts to develop more engineer-managers or project engineers who can direct the successful development of intricate engineering systems, who can deal with new orders of reliability, who can bring wisdom and social foresight to the difficult task of handling technological change so that it benefits and does not hurt people, and who can mobilize technology with this in mind to increase productivity.

10) Do not misuse science and technology by distorting them for propaganda purposes. We will build greater prestige in the long run by insuring the quality, vigor, and integrity of our science and technology. We gain prestige by being better in more areas.

11) Encourage more scientists and engineers to prepare themselves for foreign service and for advisory and administrative responsibilities in government. Encourage universities to establish programs to educate scientists having this orientation. . . .

News Notes

New Congress Will Consider Many Conservation Issues

The new session of Congress promises to be an interesting one for conservationists, according to the National Wildlife Federation, for the Kennedy Administration is expected to launch new programs and develop different approaches to old ones. Until the inauguration on 20 January, Congressional activity will be principally devoted to reorganizing; the composition of most committees will change in both the House and Senate.

As always at the beginning of a new session, a host of bills will be introduced. Earliest consideration, however, may be directed to the budget. Conservationists will be especially interested in appropriations for water pollution control, chemical pesticides research, recreational facilities in national forests, fire-ant control, and public works, such as dam construction. No bills are carried over from the 68th Congress, and all proposals, including re-introductions, will be given new numbers and taken through the entire legislative process.

Some of the Issues

Some of the major conservation issues that probably will come before the 87th Congress are as follows.

Water pollution control. Several members of the Congress already have announced their intention to introduce bills to amend the Federal Water Pollution Control Act. At least one proposal, by Congressman John A. Blatnik (Minn.), probably will include increasing the authorization for federal grants to municipalities for construction of waste-treatment plants; strengthening federal law-enforcement authority in this field; and upgrading the status of the federal water pollution control program within the Department of Health, Education, and Welfare.

Oil pollution treaty. The Senate may be asked to allow the U.S. to accede to terms of the 1954 London Convention Relating to Pollution of the Seas by Oil. Such a proposal won the approval of the Senate Committee on Foreign Relations last year but did not reach the Senate floor.

Waterfowl wetlands. New proposals leading to the acquisition of waterfowl wetlands in both the U.S. and Canada may be introduced. Congress may be asked to authorize the Bureau of Sport Fisheries and Wildlife an advance loan for the immediate acquisition of U.S. wetlands, the funds to be repaid from sales of duck stamps.

Land retirement. In any farm program which proposes land retirement as a means of coping with the crop surplus problem, conservationists will be interested in the establishment of conservation practices, including those of particular benefit to wildlife.

Wilderness preservation. Additional consideration of the establishment of a Wilderness Preservation System probably will continue along lines of S. 3809 and H.R. 12951, so-called "clean" versions of the proposals which were introduced shortly before the 86th Congress adjourned last fall.

Multiple-use policy for public domain. Congress, which last year directed that national forests be managed in accordance with multiple-use principles, probably will be asked to establish a similar policy for public domain properties administered by the Department of the Interior.

Pesticide chemicals. Efforts to establish a "Chemical Pesticides Coordination Act," similar to one proposed in a bill which failed to pass the 86th Congress, are anticipated.

Automation of Industry Is Soviet Goal

The Soviet Union is launching a major effort to ultimately convert its industrial production to automation, according to a recent report by the Mathematics Center at the Martin Company's Research Institute for Advanced Studies (RIAS) in Baltimore. An 11-man panel has surveyed recent Soviet contributions to mathematics, evaluating research and attempting to identify special features that indicate the objectives of Soviet science. The panel concludes:

"There is reason to believe that the U.S.S.R. can achieve a rapid acceleration in its rate of technological progress by an all-out scientific program in the field of automatic control. It seems clear that they intend to make the effort and it is unwise to assume that they will not be successful."

This warning of a Russian bid for world supremacy in industrial production was based on 12 months of intensive study of Russian scientific journals and books, and on personal contact and scientific correspondence with Russian mathematicians over a period of years. Joseph LaSalle of RIAS, chairman of the special panel, said that the field of Russian mathematics is revealing "because the level of mathematics of a country is an important measure of the strength of its science and technology."

The panel concluded that "in mathematics the Soviet Union and the United States lead the world and are about at the same level." But the 350-page report predicts that the Soviet Union will move at a faster rate than the United States in advancing the application of mathematical theories because communication seems to be better between Russian than between American mathematicians and engineers.

Pointing out that all too many American mathematicians write only for each other, the report states, "Leading Soviet mathematicians have an interest in and contribute to both pure and applied mathematics. Soviet mathematicians make serious and successful efforts to communicate the latest theoretical advances to engineers and scientists."

The panel members surveyed the following fields of mathematics: algebra, control and stability, functional analysis, numerical analysis, probability and statistics, partial differential equations, and topology. (RIAS had previously published a study on Soviet nonlinear differential equations, by Solomon Lefschetz and LaSalle.) The detailed studies for each field will be published in book form in 1961 by the Macmillan Company.

Salary, Employment, and Education Data Released by Science Foundation

More than 110,000 scientists have answered a National Science Foundation questionnaire that is providing a statistical profile of the salary, experience, education, age, and other characteristics of this country's scientists. The data are being gathered and processed by the foundation's National Register of Scientific and Technical Personnel.

A preliminary report shows that in 1960 scientists had a median annual salary of $9000. The highest median salaries were earned by those employed in industry, those with a doctorate,

and those engaged in management or administrative duties.

Nearly half of the registrants reported that their foremost specialty was either in chemistry or the life sciences (agricultural, biological, and medical). Ten percent designated physics, and 9 percent mathematics. The largest single field designated as the foremost specialty was chemistry.

Sixty percent of the employed scientists indicated they held advanced degrees; 37 percent had the doctorate, and 23 percent had the master's.

Although the median age for full-time employed scientists was 38, one-fourth reported that they had had 20 or more years of professional experience; 60 percent, from 5 to 19 years.

The National Register of Scientific and Technical Personnel has been maintained by the foundation since 1953 to make available timely information on the supply and professional characteristics of scientific personnel in important fields. The questionnaires are circulated by scientific societies: the American Chemical Society, the American Geological Institute, the American Institute of Biological Sciences, the American Institute of Physics, the American Mathematical Society, the American Meteorological Society, the American Psychological Association, and the Federation of American Societies for Experimental Biology. Information from a total of about 250,000 scientists is expected.

Water Pollution Conference Recommends National Goals

Some 1200 people assembled in Washington, D.C., 12–14 December, for the National Conference on Water Pollution called by the U.S. Surgeon General at the request of President Eisenhower. (Registration undoubtedly would have been higher but for a severe snow storm.) The conference was organized to include a day of plenary discussions and a banquet, a day devoted to four separate panel discussions, and a day for summations. Virtually all water-use interests were well represented.

Although no formal votes were taken on conclusions, the four panel discussions developed 31 recommendations for the Department of Health, Education, and Welfare to consider in preparing a summary of the conference. The recommendations are to be condensed into the water pollution control goals, together with suggested programs, requested by Arthur S. Flemming, Secretary of HEW.

Recommendations

Panels 1 and 3 recorded their conviction "that the goal of pollution abatement is to protect and enhance the capacity of the water resource to serve the widest possible range of human needs, and that this goal can be approached only by accepting the positive policy of keeping waters as clean as possible, as opposed to the negative policy of attempting to use the full capacity of water for waste assimilation."

Panel 2 recommended adoption and publication of a national credo, that "(i) users of water do not have an inherent right to pollute; (ii) users of public waters have a responsibility for returning them as nearly as clean as is technically possible; and (iii) prevention is just as important as control of pollution."

These basic statements of philosophy, also enumerated in a plenary-session address by Ira N. Gabrielson of the Wildlife Management Institute, were objected to by a representative of the National Association of Manufacturers. He suggested modifications to make allowance for economic feasibility.

Panel 1 also recommended that the "public policy formally recognize the recreation value of our water resources as a full partner with domestic, industrial, and agricultural values in water quality management policies and programs."

Other recommendations were for more research, particularly into the relatively new fields of radioactivity, chemical pesticide, and thermal pollution; greater control of pollution from federal installations; increased dissemination to the public of pollution-control information; comprehensive watershed planning to include location of industrial sites and systematic stream-flow regulation; development of water-quality criteria and monitoring; recognition of soil conservation, sediment control, and salinity control as pollution abatement measures in resource-development programs; and realization of the value of federal grant-in-aid programs. Discussions revealed that differences of opinion exist concerning the extent to which the federal government should be committed for financial help in the construction of waste-treatment plants and for enforcement of water-pollution laws.

The four members of Congress who addressed conference participants at the banquet—Senators Robert S. Kerr (Okla.) and Francis Case (S.D.) and Representatives John A. Blatnik (Minn.) and William C. Cramer (Fla.)—said they would introduce or support legislation to amend the Federal Water Pollution Control Act. However, their approaches to the pollution control problem would differ.

News Briefs

U.S.–Chilean antarctic program. A cooperative program of antarctic research supported by the governments of Chile and the United States has been announced by the National Science Foundation. Five U.S. scientists recently left Valparaiso aboard a Chilean naval vessel to launch the program.

The United States will help Chile establish geomagnetic research at the Presidente Gabriel Gonzales Videla station by providing geomagnetic observing equipment. Chile, in return, will assist a U.S. expedition on the Palmer Peninsula by providing transport and helicopter support throughout the present antarctic summer.

* * *

Industrial research increases. Private industry spent $9.4 billion for research and development in 1959, the National Science Foundation reports. This was 15 percent higher than the 1958 level and represents a continuation of an upward trend. However, estimates of such expenditures supplied to NSF by industrial firms indicate a somewhat smaller annual increase in 1960 (8 percent) than in 1959. More than half (57 percent) of the industrial research and development funds in 1959 came from the federal government.

* * *

Protozoology. The first International Conference on Protozoology, arranged under the auspices of the Czechoslovak Academy of Sciences, will be held jointly with the 13th meeting of the Society of Protozoologists in Prague, 22–30 August 1961. Each session will consist of one or two general lectures by outstanding protozoologists invited by the Czechoslovak Academy and of short contributed papers. Simultaneous translation facilities will be provided.

Contributed papers are invited from all those interested, regardless of membership in the Society of Protozoologists. In the Western Hempshire, inquiries should be sent to the acting

secretary, Dr. Norman D. Levine, College of Veterinary Medicine, University of Illinois, Urbana, Ill. The abstract deadline at Urbana is *1 March 1961*. In the Eastern Hempshire, communications should be sent to Prof. Otto Jirovec, Charles University, Vinicna 7, Praha II, Czechoslovakia. The abstract deadline in Prague is *1 April 1961*. Those who wish to attend the meetings but do not wish to present a paper should write Jirovec to this effect, regardless of where they reside.

* * *

Biology film preview. At a recent preview, Roman Vichniac of Yeshiva University, research biologist and well-known photographer of microscopic life, showed the initial reel in the "Living Biology" experimental film series he is preparing to improve biology instruction in high schools and colleges across the nation. The film, "The Living Tide," is the first of 13 16-mm sound-color films to be produced under an 18-month grant from the National Science Foundation.

Scientists in the News

Rudolf L. Mössbauer, research fellow in physics at California Institute of Technology, has won the 1960 Research Corporation Award for discovering the radiation effect that now bears his name, the "Mössbauer effect." Mössbauer, who is on a 2-year leave from the Institute of Technical Physics in Munich, Germany, will receive the $5000 award on 19 January at the Research Corporation's annual dinner, at the Sheraton East Hotel, New York.

Rudolf L. Mössbauer

The editors of *Time* magazine have named 15 scientists as U.S. "Men of the Year," whose work "shapes the life of every human presently inhabiting the planet." This 34th annual selection of men or women who have "dominated the news . . . and left an indelible mark—for good or ill—on history" is the first in which more than one person has been named, except for 1937 when General and Madame Chiang Kai-shek were chosen. The 1960 "representatives of all science" who are featured in *Time*'s issue of 2 January are as follows:

Robert Woodward, 43, Harvard's Nobel Prize winner, is known for his syntheses of quinine, cholesterol, and, in 1960, chlorophyll.

Charles Stark Draper, 59, of Massachusetts Institute of Technology, is the aeronautical engineer largely responsible for the development of the inertial guidance systems that control far-ranging U.S. missiles, including the Polaris.

William Shockley, 50, physicist, earned a Nobel Prize, with two colleagues, for creating the transistor.

Emilio Segrè, 55, physicist, did much of his early work in his native Italy, collaborating with the late Enrico Fermi in perfecting the slow neutron process essential to production of the atomic bomb. He won a Nobel Prize for his research on anti-matter.

John F. Enders, 63, virologist associated with the Children's Medical Center in Boston, won a Nobel Prize for developing a poliomyelitis vaccine.

Charles Townes, 45, currently on leave from Columbia University to work at the Institute for Defense Analysis in Washington, is noted for his work with microwaves and his contributions to the development of the maser.

George W. Beadle, 57, Nobel Prize-winning head of the biology division at California Institute of Technology, initiated genetic investigations that led to the first explanations of the manner in which genes control enzymes and enzymes control the basic chemistry of life.

James Van Allen, 45, cosmic ray specialist at the State University of Iowa, conducted experiments with rockets and satellites that demonstrated the existence of the Van Allen radiation belts that girdle the earth.

Edward Purcell, 48, now on leave from his job as a Harvard physicist, won the Nobel Prize for his "nuclear resonance" system for measuring atomic properties. He has a special talent for reducing the complexities of science to understandable simplicity.

Edward Teller, 53, Hungarian-born physicist at the University of California, is best known for his contributions to the development of the H-bomb.

Willard Libby, 52, of the University of California at Los Angeles, received the 1960 Nobel Prize for his work with radioactive carbon dating.

Isidor I. Rabi, 62, now a part-time professor at Columbia University, won a Nobel Prize in 1944 for experiments in molecular physics which were vital to U.S. atomic research.

Linus C. Pauling, 59, Caltech chemist, won a Nobel Prize in 1954 for his chemical bond theory.

Joshua Lederberg, 35, won a Nobel Prize in 1958 for his discovery that bacteria infected with certain viruses may suffer hereditary changes. Now at Stanford's School of Medicine, he is concerned with exobiological research, with the ultimate objective of comparing the patterns of chemical evolution of the planets.

Donald Glaser, 34, of the University of California at Berkeley, received this year's Nobel Prize for his invention of a liquid hydrogen bubble chamber for photographing atomic particles. He is now conducting research in microbiology.

Roger Revelle, director of the University of California's Scripps Institution of Oceanography for the past decade, has been chosen dean of the university's new School of Science and Engineering in San Diego. Revelle retains his position as director of Scripps.

The school, designed to provide graduate instruction and basic research in the sciences and engineering, opened its doors to graduate students for the first time in September. Departments of physics, chemistry, and the earth sciences are already in operation. Other departments are planned. The school is the university's first step toward the establishment of a large general campus in the San Diego area.

Roland Dietz, of the Max-Planck Institut für Meeresbiologie, Abteilung Bauer, Wilhelmshaven, Germany, is serving as visiting professor of cytology at the Dartmouth Medical School for approximately 6 months. Using the rectified polarizing microscope, he is studying the fine structure of living spindle fibers and kinetochores in tipulid fly meiosis.

Joanne S. Malkus, meteorologist at the Woods Hole Oceanographic Institution, Woods Hole, Mass., has accepted a professorship in the department of meteorology at the University of California, Los Angeles. She goes to her new post in January.

Charles A. Doan became dean emeritus of the College of Medicine at Ohio State University on 1 January. He remains a professor in the college. The former associate dean, **Richard L. Meiling**, has assumed the deanship.

William P. Shepard, who is retiring shortly as chief medical director of the Metropolitan Life Insurance Company, has accepted the office of associate director of the Institute for Advancement of Medical Communication (in New York), a nonprofit organization engaged in developing improved methods for communication within and between disciplines in the health sciences.

Wayne State University has created a university professorship with the aid of a $110,000 grant from the McGregor Fund. **John M. Dorsey**, internationally known psychiatrist, is the first appointee. He will leave the chairmanship of the psychiatry department at the College of Medicine to assume his new duties on 1 February.

As presently conceived, the university professor will not be attached to a specific department; rather, as "generalist" for the whole academic community, he will be responsible for a limited number of regular credit courses of wide usefulness to the student body and also for bringing to the campus, as lecturers and visitors for the benefit of the students, men who have "wholeness of vision."

John C. Cutler, U.S. Public Health Service specialist in venereal disease control, has been appointed assistant director of the Pan American Sanitary Bureau, regional office of the World Health Organization in Washington, D.C. For the past year he has been assigned to the Allegheny County (Pa.) Health Department as director of its Central Health District. He has also been adjunct associate professor of public health practice at the University of Pittsburgh.

Cutler is succeeded in the Allegheny County post by **Warfield Garson**, who has been director of the PHS Venereal Disease Experimental Laboratory in Chapel Hill, N.C., since 1955.

John R. Amberg, director of radiology at Milwaukee County Hospital, Milwaukee, Wis., has been appointed associate professor and chairman of the new department of diagnostic radiology in Marquette Medical School's Radiology Division. The division also has a newly established department of radiation therapy, which will be headed temporarily by division chairman **S. B. Morton**.

Clark K. Sleeth, long-time member of the medical faculty at West Virginia University, has been appointed dean of the institution's School of Medicine, effective 1 January. He succeeds **E. J. VanLiere**, who reached retirement age last October but has remained in the position of dean. Sleeth is a specialist in gastrointestinal physiology.

The American Society of Agronomy presented its three highest awards during its recent meeting in Chicago.

Michael Peech of Cornell University received the society's soil science award; **S. T. Dexter** of Michigan State University, the crop science award; and **J. K. Patterson** of Washington State University, the agronomic education award.

John C. R. Kelly, Jr., formerly manager of the technology department of the Westinghouse research laboratories, has been named to the newly created position of director, centralized technical services, of the Westinghouse central laboratories. In this position he will consolidate and administer the technical services formerly supplied by separate departments of the research laboratories and the Westinghouse materials laboratories. These laboratories are among those being brought together with the new products laboratories, the headquarters design laboratories, and the patent department into a new Westinghouse research and development center now under construction in Churchill Borough, near Pittsburgh.

Nisson A. Finkelstein, research physicist, has been appointed vice president in charge of research for the Stromberg-Carlson Division of General Dynamics Corporation, Rochester, N.Y., effective 1 January. He joined Stromberg-Carlson in 1959 as assistant vice president and director of research.

F. Eugene Nelson, formerly professor of dairy science at Iowa State University, has joined the University of Arizona's College of Agriculture.

Recent Deaths

Mark Balderston, Easton, Pa.; 71; professor emeritus of physics at Lafayette College, where he served from 1926 until his retirement in 1959; 19 Dec.

Eric Temple Bell, Watsonville, Calif.; 77; emeritus professor of mathematics at California Institute of Technology and a specialist in the theory of numbers, who developed several important theorems; in addition to many technical papers and several well-known textbooks, wrote popular works in mathematics, including a series of science-fiction novels under the name of John Taine; was working on a book about the 7th-century French mathematician Fermat; was a member of the National Academy of Sciences, a former president of the Mathematics Association of America, and a former vice president of the physical science section, AAAS, and of the American Mathematical Society; former editor of various scientific journals; 20 Dec.

Martin R. Huberty, Los Angeles, Calif.; 66; acting dean of the University of California's College of Agriculture at Los Angeles, director of the Water Resources Center, and professor of irrigation, soil science, and engineering; 12 Dec.

Karl Lehmann, Basle, Switzerland; 66; archeologist and professor at the Institute of Fine Arts of New York University; since 1938 had directed the expedition excavating the ancient Greek religious sanctuary on the island of Samothrace, in the Aegean Sea, under the auspices of N.Y.U. and in cooperation with the American School of Classical Studies in Athens; an authority on Greek and Roman art, archeology, religion, and philology, he wrote a number of books, among them a definitive work on Trajan's column in the Forum of Trajan, a three-volume study of ancient bronzes, and a book on the ancient ports of the Mediterranean; 17 Dec.

Valy Menkin, Kansas City, Mo.; 59; head of the pathology department of the dental school at the University of Kansas City; former head of the experimental pathology department at the Temple University School of Medicine; member of the Royal Society of Medicine in London; had isolated nine substances in investigations of various biological manifestations of inflammation and was the first to demonstrate the anti-inflammatory property of cortisone; 13 Dec.

Book Reviews

The Eskimos. Kaj Birket-Smith. Translated from the Danish by W. E. Calvert. Foreword by C. Daryll Forde. Methuen, London; Humanities Press, New York, rev. ed., 1960. xiv + 419 pp. Illus. $6.50.

The Story of a Tlingit Community: A Problem in the Relationship between Archeological, Ethnological, and Historical Methods. Frederica de Laguna. Smithsonian Institution, Washington, D.C., 1960 (order from Supt. of Documents, GPO, Washington 25). vii + 254 pp. Illus. $2.

An Eskimo Village in the Modern World. Charles Campbell Hughes. Cornell University Press, Ithaca, N.Y., 1960. xiv + 419 pp. Illus. $6.75.

As favorite subjects of science and literature for over five centuries, the Eskimos have become a physical and cultural benchmark for studies of other members of our species. This revised edition of Birket-Smith's classic work, first published in English in 1936, is a convenient survey of the Eskimo-Aleut stock and the vast scientific literature about them. His study benefits from his own diverse anthropological researches among Eskimos in southern Alaska, northern Canada, and Greenland. After the foreword by C. Daryll Forde, the major categories of history of discovery, ecology, physical characteristics, language, economy, cultural adaptations to cold, social structure, psychology, archeology, cultural history, and changes contingent upon contact with European cultures are reviewed. This treatment affords an excellent syllabus for courses on the Eskimo-Aleut stock.

There are some seven recurrent themes whose revision would justify a third edition:

1) For *Eskimo* the reader must frequently read *Eskimos of northern Canada and Greenland*. The author's greatest descriptive concern lies with the "typical" impoverished minority of arctic Eskimos, scrabbling for a meager existence amid ice, snow, and dogs, while the "atypical" and less gelid majority luxuriate in the subarctic regions, contaminating their culture by trafficking with Indians to the south or by smuggling alien traits in through Russia. It should be reiterated that less than 10 percent of the stock have ever seen a snow house, three-fifths of them live south of Bering Strait, and the majority have always lived in the subarctic.

2) The splendid chapter, "Fighting the cold," contains no reference to the many physiological studies of cold adaptation, or to such things as childhood training aimed at inuring them to cold, which is practiced by several thousands of Eskimos and Aleuts who risk the hazard of hypothermia involved in the extensive use of kayaks in cold water, not in ice or snow.

3) Regional variations are minimized, especially contrasts between east and west. These include important major differences in population size, length of life, and cultural complexity, all of which are substantially greater in the western area and especially in southwestern Alaska and the eastern Aleutians.

4) The consequences and correlates of population size, genetic or cultural, are not elucidated. Complex and rich cultures are not possible without numerous and permanent villages and large numbers of people. Therefore they cannot exist in the absence of suitable ecological foundations. The central arctic has long been an extremely difficult place to make a living and has had only a sparse population. Here the use of dogs is a vital necessity. Dependence on the dog has involved an interacting series of commitments, so that there is some question of whether the dogs work for the Eskimos or vice versa. Dogs eat large amounts of the same food the Eskimos eat. To work effectively, a sled dog must be fed daily, whereas a kayak, at most, "takes only a little water."

5) Similarities with inhabitants of the Northwest coast are automatically considered to be evidence of diffusion from Indians to Eskimos, rather than either diffusion from Eskimos to Indians or derivatives of an older stratum common to larger areas.

6) Remote areas are frequently suggested as possible sources for traits, and connections with Sumer and the Upper Paleolithic of western Europe are maximized at the expense of local cultural history and the well-known inventiveness of the Eskimos and Aleuts.

7) An important equation, "Arctic coast culture proper . . . is actually the typical Eskimo culture," leads to the suggestion that this adaptation took place in the central arctic, and that the subarctic Eskimos and Aleuts (some 64,600) and the high arctic culture (less than 300 Eskimos) are later offshoots.

Better evidence has existed for some time now, and was cited as early as 1871 by Lewis H. Morgan, for a major dichotomy between Eskimos and Indians in both physical traits and culture, and for archeologically derived similarities in material culture between the coastal areas of northern Japan and Siberia and the eastern shores of the Bering Sea and the Pacific Ocean. All of the following indicate that much of the synthesis of the Eskimo-Aleut culture took place in western Alaska: linguistic diversity; early carbon-14 datings; the early appearance of lamps, labrets, boats, bird spears, and so forth; and Mongoloid skeletons found in western Alaska, as well as the greater ecological wealth and the broader population base and, therefore, population size (deep, stratified village cites indicating permanence and continuity). Certainly one major area was the triangle between Nunivak Island, Kachemak Bay, and Umnak Island in the Aleutians.

Concerning omissions and errors, there is no reference to J. B. Jørgensen's excellent studies of the Eskimo skeleton, or to W. Goldschmidt's studies of culture change, particularly of revisions in the criminal code in Greenland. Part of the notable success of the Danes in administering the Eskimos of Greenland lies in the combination of good scholarship with good will. One factual error is the statement that all Aleuts were evacuated to the Alaskan coast prior to

the Japanese invasion of the Aleutians. In fact, the entire village of Attu was captured and removed to northern Japan. After liberation the American authorities did not permit them to return to their home but installed them in Atka. Few books on the Eskimos deserve more serious study than this one by Birket-Smith.

Tlingit Culture

Frederica de Laguna's critical examination of the history of Angoon, a Tlingit Indian community in southern Alaska, employs carefully collected archeological, ethnological, and historical data; it is a superb study in method with the immediate application of the methods of analysis and criticism. The over-all aim of de Laguna's studies, made over a period of several years, has been to trace the development of Tlingit culture from the earliest period represented by discoverable remains down to the present and to provide not only a descriptive history but insight into cultural dynamics. This monograph provides a comprehensive statement of all that she and her colleagues have learned about the archeology of the Angoon area and that part of the ethnographic information that bears upon the archeology. Although the basic data for this study were gathered during the summers of 1949 and 1950, the author also draws upon data which she and her long-standing colleague, Birket-Smith, collected as early as the 1930's in southern Alaska.

The special character of this work derives from the combination and analysis of archeological, ethnological, and historical data (and this gathered by one person), together with a lucid discussion of premises and procedure. Sources of bias, including sample errors, to which archeologists and ethnologists are variously prone receive prominent attention. The first 23 pages could well be reprinted and carried by all such investigators as part of their field equipment, regardless of the geographical area being investigated. (But it would be preferable to read it before entering the field.)

An initial assumption is that certain continuities of pattern, distinctively Tlingit, can be traced historically; another is that exploration of the relationship between archeology and ethnology could be accurately perceived only through concern with the culture as a totality. The most distinctive assumption, uncommonly rare and rarely hinted at in contemporary studies of culture change concerned with the breakdown of old cultures, is that the Tlingit themselves are as much responsible for their own culture and its history as any of the people who have influenced them. Even today these Indians are not passive recipients of foreign teachings, rather, "It has been Tlingit character, interests, and orientations that have determined how these importations were re-interpreted to fit Tlingit ethos and adjusted to Tlingit culture" (page 8). Accordingly, it was necessary to secure the Tlingit point of view—their concepts of history, geography, and systems of explanation. Further, it was necessary to secure a record of actual behavior as manifested in what the Tlingit have actually done in particular situations and what they have done it with, as shown by the artifactual record. The ever-recurring problem of assessing verbal behavior is treated throughout, but it is especially well illustrated by the story of the alarm aroused when a family of bears moved into the neighborhood. This provoked much excitement and many expressions of serious concern, but despite the abundant verbal expression of anxiety, the children bicycled and the women and children gathered berries in the bear haunts.

When de Laguna cites generic characteristics of the Tlingit—such as their reserve and shyness, their lack of interest in the customs of other tribes, their limited interest in certain aspects of anatomy, their great concern with their own individual ancestors and not just famous Tlingits, their orientation about sibs, the cleanliness of the villages, and their concern with specific locations rather than areas—the reader will find convincing evidence as tangible as that of the stone and bone artifacts. It is interesting to note that the artifactual record is somewhat meager. No large sites have ever been reported from the Tlingit area, and the total body of evidence suggests that the story of Angoon may be contained within the last 160 years. The problems common to archeologists and ethnologists obviously consist of much more than the verification of native stories by use of the spade. A thorough description is given of village sites, forts, and temporary sites, as well as information concerning artifacts, food resources, and the physical situation; there is an analysis of the Tlingit names and accounts of events which took place in the immediate area. Such information provides excellent material for the archeologist, ethnologist, historian, and traveler, as well as for those interested in methods of analysis and criticism of such data.

Social Change

Various trends related to the impact of the industrialized world on a small nonindustrialized community constitute the principal object of Hughes' study of Gambell, which is situated on the northwest corner of St. Lawrence Island in the Bering Sea. "The general theme underlying all these trends forms the most important focus for the present study: the nature of the relationship between the small sociocultural world and the mainland." Comparisons are made with the condition of the village in 1940; and the assumption is made that Gambell was an Eskimo village in that year, whereas by 1955 the dominant culture had become that of the mainland world of the white man.

A large amount of useful data—on village social organization, interpersonal relations, contact with Europeans, government agencies, health problems, food consumption, and the economy—is presented along with a relatively large number of quotations from European authors concerned with social problems and social pathologies. Analyses of the culture as such, of the intellectual world of these Eskimos, or of many parts which would require conversancy with the Eskimo language or linguistic analysis, are not a primary concern. Inclusion of the actual corporate genealogy of Gambell and of Angoon (studied by de Laguna), including numbers of living and dead children of each mating, would have made possible genetic analyses, as well as analyses of aspects of differential fertility and would also have permitted comparison of the formal kinship system against the actual biological matrix on which the village is constructed.

The reader may involuntarily recall A. L. Kroeber's generic permanent review of such studies: "Acculturation studies in particular, at any rate as they are conducted in America, seem particularly monotonous and depressing, equally so whether the acculturees are ethnic minority immigrants or ethnic remnant aborigines. These unfortunates always emerge from the process as bot-

tom-level members of our own society and culture. . . . Yet each study appears to be the repetition of a principle akin to the one that when a bulldozer meets the soil that nature has been depositing for ages, the bulldozer always and promptly wins" ("What ethnography is," vol. 47, No. 2, University of California Publications in American Archaeology and Ethnology, University of California Press, Berkeley, 1957). Hughes illustrates the last 15 years of this bulldozing operation, and in his final chapter, "The broken tribe," offers a suitable obituary.

WILLIAM S. LAUGHLIN
Department of Anthropology, University of Wisconsin

La Culture des Tissus Végétaux. Techniques et réalisations. R. J. Gautheret. Masson, Paris, 1959. iv + 884 pp. Illus. F. 10,500.

For 30 years I have been a friend and a friendly rival of the author whose work is under consideration. Under these circumstances, a completely objective treatment of the work is scarcely possible, and it is with much hesitation that I have accepted the task assigned to me.

This book is not a handbook. It is an encyclopedia. In its six sections—"Techniques"; "Morphogenesis"; "Polarity and induction"; "Physiology"; "Cultivation of isolated cells"; and "Pathology"—Gautheret brings together in one volume much of the important work on the in vitro cultivation of plant tissues, up to 1958. These sections are all treated in detail, with a wealth of illustrations and specific citations. All represent fields in which the author or his students have made important contributions. With its bibliography of 986 titles, this will be an indispensable reference for all workers in the field for many years to come. It stands as a monument to Gautheret's leadership.

Perhaps the strongest parts of the book are the sections on morphogenesis and polarity, in which are found imaginative and exhaustive analyses of tissue relations, both in primary explants and in established strains; of the effects of the various growth substances; and of the differences between species, between types of organs serving as sources of explants, and between materials associated in different ways. This is the type of work in which the author is most at home, and it is excellent.

Yet, having given this praise, I must confess to an uneasy feeling that the treatment is so personal that the book lacks much of the objectivity one expects in a general treatise. True, the author warns us when he says, in his introduction to chapter 1: "We do not propose to describe all the techniques employed in the cultivation of plant tissues but to emphasize the procedures used in our own laboratory or developed by our pupils" (page 10). These limitations extend to much more than technique; they permeate the entire work.

Nowhere is there a clear definition of what is or is not to be considered a "plant tissue culture." There is no historical section which might serve to place this question in perspective. Nor does the treatment itself help. Cultures of roots, stem tips, embryos, pollen-mother-cells, and other organized materials are brought in only when they have served as sources of disorganized masses. This results in the omission of much that has contributed to the development of the field.

On the other hand, large parts of the sections on morphogenesis, polarity, physiology, and pathology deal with phenomena which can only be effectively studied in primary explants, masses which may or may not give rise to permanent cell cultures but which often produce roots and stem tips and are capable of serving as sources of complete plants—that is, as cuttings. Inclusion of such materials expands the term "tissue culture" far beyond that usually accepted. The feeling emerges that to Gautheret a "tissue culture" is anything studied in his laboratory, and that anything studied elsewhere is important only so far as it supplements his own work.

This chauvinism crops out repeatedly. Gautheret attributes the "establishment" of tissue culture to Alexis Carrel (page 733), an idea which would certainly be opposed by the proponents of Ross Harrison. He describes and illustrates (page 283, Fig. 143), as if it were an original discovery (1934), the disorganization of cultivated root tips as a result of injury, ignoring Chamber's earlier description (1925) and my discussion and illustration of the same phenomenon (1932), although he cites both of these papers elsewhere. He states that Heller's nutrient is "of almost universal use" (page 15); this may be true for France, but it is certainly not true for many laboratories in America, Asia, and Europe (elsewhere than in France). This is a French work, a Parisian one, but not a well balanced international one.

There are some curious statements. Gautheret says that dry sterilization of glassware should be avoided since it renders the surfaces alkaline (page 82); this is certainly untrue of clean Pyrex, which is used extensively elsewhere. He says, "Petri dishes must not be used for subcultures" (page 63), although such use is quite extensive. He says that aluminum foil should never be used for capping tubes (page 64); this method is widely approved. On the other hand, none of the watch-glass methods are described, nor is the method of cultivation in pharmaceutical bottles of various sorts, developed, especially in Riker's laboratory, because of its cheapness. The only shake-culture method described is the relatively complicated one introduced by Steward; the simpler ones of Riker and of Nickell are ignored.

In his introduction to the chapter on cultivation of single cells (page 722), Gautheret seems to have missed completely the real significance of Haberlant's reason for suggesting the cultivation of plant cells (1902). And because of the resulting limited concept of the objectives of single-cell cultures, he misunderstands (pages 727–28) the nature and significance of Steward and Schantz's observations on the organization from disaggregated cells, first of cell masses and then of roots and stems; these observations, by the way, were made many years before, though under less well controlled conditions, by both Nobécourt and Levine.

The proof reading is generally excellent, but there are several curious slips. On page 774, in discussing Braun's tobacco teratoma studies, the word *feuilles* is used twice where I am sure *tiges* is meant. On page 278 *Iris* should be *onion*. And on page 290 (the caption for Fig. 146, last line) *bas* should evidently be *haut*.

One of the sections which most raised my hackles was the discussion of growth regulators (page 653). Here the author says: "Since the first attempts of Robbins and of White with yeast extract, the study of the activity of natural products has made little progress. . . . Attempts to extract active components contained in such products have failed. . . . These investigations have led to a situation comparable to that of the

attempts to isolate the trephones for animal tissue cultures. Instead of leading to definite substances these studies have only established the fact that animal cells require many materials involving complex synergies. The future will tell if the same is true for plant cells." In my judgment this statement is untrue for either plant or animal cells. It seems to ignore all the work carried out between 1922 and 1940 by Robbins, Bonner, and White in which, beginning with yeast extract, there were established fully defined nutrients that are used today in dozens of laboratories for the cultivation of a very wide variety of plant tissues. And it ignores the parallel studies made between 1940 and 1958 by which Fischer, White, Morgan, and Parker; Earle and his colleagues; and Waymouth arrived at equally effective defined nutrients for animal cells. Carrel's "trephones" have been relegated to the limbo of "phlogiston," but Gautheret seems to be unaware of that fact.

The bibliography, in spite of its length, is also incomplete.

All of these biases makes one wonder a bit about the depth of the work. Massive it is. It will be very useful. But it is a highly personal work, and the reader should be warned that he will not always find therein completeness or objectivity.

PHILIP R. WHITE
Roscoe B. Jackson Memorial Laboratory, Bar Harbor, Maine

Advances in Organic Chemistry. Methods and results. vol. 2. Ralph A. Raphael, Edward C. Taylor, Hans Wynberg, Eds. Interscience, New York, 1960. vii + 503 pp. Illus. $15.

This is the second volume in a series aimed at giving organic chemists critical evaluations of the newest methods and ideas in organic chemistry; it so admirably fulfills this purpose that, in most cases, the experimenter can go directly from the book to the laboratory when application of one of the new techniques fits his problem. Internationally known chemists discuss and evaluate the following topics: the uses in synthesis of alkenylmagnesium halides (H. Normant); dialkoxy dihydrofurans and diacyloxy dihydrofurans (N. Elming); ethynyl- and thioethers (J. F. Arens); ketene (R. W. Lacey); nuclear magnetic resonance in structure determination (H. Conroy); hydrogenation-dehydrogenation reactions, including enzyme systems (L. M. Jackman); ultraviolet photochemistry (P. de Mayo); and the chemistry of muscarine (C. H. Engster).

RICHARD H. EASTMAN
Department of Chemistry, Stanford University

Middle American Anthropology. vols. 1 and 2. Special symposium of the American Anthropological Association. Social Science Monographs 5 and 10. Assembled by Gordon Willey, Evon Z. Vogt, and Angel Palerm. Social Science Section, Pan American Union, Washington, D.C., vol. 1, 1958; vol. 2, 1960. 60 pp. and 73 pp.

These monographs offer a collection of papers and comments concerning an appraisal of anthropological research that has been carried on in Middle America for the past 50 years. The topics were selected by Willey and Vogt, and in the introduction they say that "the authors of the principal essays were asked to make a survey of the past, an evaluation of the present, and speculation for the future."

Contents of volume 1 are "Middle American archaeology since 1906" by A. V. Kidder, with discussions by Robert Wauchope and George W. Brainerd; "Regional sequences in Mesoamerica and their relationships" by Gordon F. Ekholm, with discussions by Edwin M. Shook and R. S. MacNeish; "Studies on Middle American art" by Tatiana Proskouriakoff, with discussions by Robert L. Rands, George Kubler, and Herbert J. Spinden; and "Research in Maya hieroglyphic writing" by J. E. S. Thompson, with discussions by Linton Satterthwaits, Jr., and E. Wyllys Andrews, IV.

Volume 2 contains the following papers: "The subsistence problem in Mesoamerican history" by Homer Aschmann, with discussion by Evon Z. Vogt; "Middle American linguistics: 1955" by Norman A. McQuown, with discussions by Morris Swadesh and J. Alden Mason; "Middle American ethnography" by Pedro Carrasco, with discussions by Arden R. King and O. G. Simmons; "Applied anthropology in Mexico" by Alfonso Caso and Gonzalo Aguirre Beltran, with discussions by Benjamin D. Paul and Allan R. Holmberg; and "Theory in Middle American ethnology" by John Gillin, with discussion by O. G. Simmons.

New Books

Mathematics, Physical Sciences, and Engineering

The Arithmetic of Computers. An introduction to binary and octal mathematics. Norman A. Crowder. Doubleday, Garden City, N.Y., 1960. 480 pp. $3.95.

Annual Reports on the Progress of Chemistry, 1959. vol. 66. Chemical Society, London, 1960. 482 pp. £2.

Boundary Layer Theory. Hermann Schlichting. Translated by J. Kestin. McGraw-Hill, New York, ed. 4, 1960. 667 pp. Illus. $16.50.

The Chemistry of Yttrium and Scandium. R. C. Vickery. Pergamon, New York, 1960. 130 pp. Illus. $6.50.

Digital Applications of Magnetic Devices. Albert J. Meyerhoff, Ed. Wiley, New York, 1960. 623 pp. Illus. $14.

Foundations of Electrodynamics. Parry Moon and Domina Eberle Spencer. Van Nostrand, Princeton, N.J., 1960. 321 pp. Illus. $9.75.

From Dualism to Unity in Quantum Physics. Alfred Lande. Cambridge Univ. Press, New York, 1960. 130 pp. Illus. $3.75.

Frequency Power Formulas. Paul Penfield, Jr. Technology Press and Wiley, New York, 1960. 176 pp. $4.

Geology of India and Burma. M. S. Krishnan. Higginbothams, Madras 2, India, 1960. 618 pp. Illus. Rs. 22.50.

Initiation à la mecanique quantique. Librairie Hachette, Paris, 1960. 336 pp. Illus.

Kernenergie—Technik. Einfuhrung in die Physik und Technik der Kernenergie—Erzeugung. Verlag Moderne Industrie, Munchen 23, Germany, 1960. 300 pp. DM. 36.

Lectures on Fluid Mechanics. Sidney Goldstein. Interscience, New York, 1960. 325 pp. Illus. $6.60.

Linear Circuits. pt. 1, *Time-Domain Analysis*; pt. 2, *Frequency-Domain Analysis*. Ronald E. Scott. Addison-Wesley, Reading, Mass., 1960. 928 pp. Illus. $6.75 each.

Markov Learning Models for Multiperson Interactions. Patrick Suppes and Richard C. Atkinson. Stanford Univ. Press, Stanford, Calif., 1960. 308 pp. Illus. $8.25.

The Mathematics of Radiative Transfer. I. W. Busbridge. Cambridge Univ. Press, New York, 1960. 155 pp. $5.

Physics of Precipitation. Proceedings of the Cloud Physics Conference, Woods Hole, Mass., 3–5 June 1959. Geophysical Monograph No. 5. Helmut Weickmann, Ed. American Geophysical Union, Washington, D.C., 1960. 447 pp. Illus. $12.50.

Precis de physique theorique moderne. Physique classique et relativiste et theorie classique des champs. vols. 1 and 2. Theo Kahan. Presses Universitaires de France, Paris, 1960. 687 pp. Illus.

Progress in Inorganic Chemistry. vol. 2. F. Albert Cotton, Ed. Interscience, New York, 1960. 409 pp. Illus. $10.50.

Tables for Petroleum Gas/Oxygen Flames. Combustion products and thermodynamic properties. I. I. Berenblut and Anne B. Downes. Oxford Univ. Press, New York, 1960. 111 pp. $4.80.

Reports

Identification of the Volatile Factor Involved in Spermatocyte Differentiation in vitro

Abstract. Ketchel and Williams postulated a "volatile factor" which participates in the differentiation of insect spermatocytes in vitro. It was found not to be a specific product of developing cysts. Instead, its effects are duplicated by a number of reagents which have only a high water content in common. The hypothesis that the volatile factor is water was experimentally confirmed.

Ketchel and Williams (*1*) have analyzed the properties of a volatile factor participating in the in vitro differentiation of insect spermatocytes into spermatozoa. This factor is of particular interest since, in the words of these authors, "the reaction between cells and hormones can generate molecules which are catalytically active and prerequisite for the biological end-result." Such an unusual and fundamental finding deserves confirmation and further examination.

Evidence for the volatile factor was based on the failure of unsealed depression slides to support differentiation and the requirement of several cultures in the same chamber when larger volumes were employed. The properties ascribed to the volatile factor, aside from its volatility, were that it was produced by the developing cells, was required by them for maximal differentiation in culture, and was eliminated from cultures by ventilation. It was insoluble in Ringer's solution, in dilute acids, in alkaline solutions, and in sucrose solutions, but was "soluble" in insect blood and "partially soluble" in mineral oil. It was absorbed by charcoal. By inference the volatile factor was neither a protein nor any other macromolecule; it was neutral, apolar, and not a normal constituent of air, such as carbon dioxide.

To identify the volatile factor we have investigated the differentiation of spermatocytes in hanging-drop cultures. The results differ from those of Ketchel and Williams (*1*), particularly with respect to the requirement for a threshold concentration of developing cysts for the production of the factor. Our results demonstrate that the volatile factor involved in spermatocyte differentiation is simply water.

Nondeveloping spermatocytes from diapausing pupae of the giant silk moth (*Samia cynthia, Philosamia cynthia* Drury, or *Samia walkeri*) were transferred to hanging-drop cultures according to the method of Schneiderman *et al.* (*2*). Blood was collected under aseptic conditions from abdominal incisions, as described by Laufer (*3*). "Inactive" blood, lacking the "growth and differentiation hormone" (presumably ecdysone, but possibly something else) was obtained from diapausing pupae. "Active" blood was obtained from individuals during the early phases of development into the adult. Blood from these animals permits spermatocyte development presumably because of its higher concentration of the "growth and differentiation hormone" (*4*).

Germinal cysts for culture were teased from testes and then checked microscopically for generally healthy appearance, sufficient concentration (a minimum of several hundred large cysts from each testis), and lack of development. The criteria for development after 5 days were those of Schneiderman *et al.* (*2*).

The volume of the culture chamber was varied by using alternatively, depression slides or two sizes of petri dishes (15 by 60 or 100 mm). Test drops containing active blood and cysts were placed on the inside of the cover, while additional drops of liquid were added either alongside the test drop or to the bottom of the dish. Each dish was sealed with Vaseline and incubated at 21° to 22°C. The number of drops of liquid as well as the nature of the liquid and its contents were varied to determine the effects of quality and quantity of fluid required for maximal differentiation of cysts under culture conditions.

The results of Ketchel and Williams (*1*) were corroborated to the following extent. (i) Single-drop depression-slide cultures of spermatocytes in active blood differentiated. An average of 42 percent of the cysts developed by 5 days (Table 1, ser. 1*a*). When a chamber was incompletely sealed, development was depressed or lacking; the culture fluid darkened and evaporated and the cysts dissociated and finally disintegrated. (ii) In larger chambers—that is, 60- or 100-mm petri dishes—single drops usually did not show signs of differentiation, while two or more (as many as four in the 60-mm dishes) yielded an intermediate percentage (0 to 12) of differentiating cysts. When a larger number of active cultures was placed in the same chamber, the percentage of differentiating cysts increased to maximal (control) levels (these values ranged between 35 and 52 percent for 6 to 16 drops; see Table 1, ser. 1*b*).

The "volatile factor" of Ketchel and Williams (*1*) was postulated mainly on the basis of observations of maximal cyst differentiation in a large chamber only when the chamber contained sufficient numbers of additional cultures also undergoing development. Thus, 16 drops of developing cultures were required to produce maximal differentiation. According to these authors, single cultures in 17-cm^3 containers resulted in 30 percent of the development seen when 16 cultures were present. Still only about 30 percent of the normal development was observed when a single drop of test cysts was cultured in the presence of 15 drops of active or diapausing blood without cysts or when 15 drops of cysts were cultured with diapausing blood alone. These additional drops did not contain developing cysts and therefore could not elaborate the volatile factor.

We repeated these experiments but obtained different results. In our experience, developing cysts were not necessary (Table 1, ser. 2). The culture chamber seems to become saturated with "volatile factor" whenever cultures of active blood and cysts are supplemented with additional drops of insect blood. It was found that there was no appreciable difference when test drops of active blood and cysts were cultured in the presence of "inactive" blood, of "active" blood without cysts, or of "inactive" blood with cysts. The feature that did appear to be significant was

Instructions for preparing reports. Begin the report with an abstract of from 45 to 55 words. The abstract should *not* repeat phrases employed in the title. It should work with the title to give the reader a summary of the results presented in the report proper.

Type manuscripts double-spaced and submit one ribbon copy and one carbon copy.

Limit the report proper to the equivalent of 1200 words. This space includes that occupied by illustrative material as well as by the references and notes.

Limit illustrative material to *one* 2-column figure (that is, a figure whose width equals two columns of text) or to *one* 2-column table or to *two* 1-column illustrations, which may consist of two figures or two tables or one of each.

For further details see "Suggestions to Contributors" [*Science* 125, 16 (1957)].

that a threshold number of drops of solution had to be present. Whether or not the inducing drops contained developing cysts made no difference in the result.

Additional experiments (Table 1, ser. 1*c* and 3) were performed to determine whether water could be substituted for "inactive" or "active" insect blood. Indeed, it was found that an equivalent amount of water could fully duplicate the effect of blood (ser. 1*c* and 3). Even in large petri dishes (ser. 3), with an estimated volume of 100 cm^3, the cysts in a single "active" drop differentiated when an excess of water was introduced into the bottom of the chamber. The cysts developed as well as control cultures in depression slides (ser. 1*a*). These experiments indicate that water can substitute fully for "active" cultures.

If water and the "volatile factor" are two independent growth factors involved in spermatocyte differentiation, then their effects should be additive, or at least they should produce significantly enhanced percentages of differentiation even at the saturation point for one of them, when the other factor is added for assay. Thus, if the two components act independently, eight drops of active cultures with an excess of water should give an appreciably higher percentage of cyst differentiation than a test culture with one drop of "active" blood and cysts with an excess of water. This expectation was not fulfilled (Table 1, ser. 4). Since either water or "active" cultures will substitute completely for the other in about the same quantity (ser. 1, *b* and *c*) and since there is no additive effect, we are forced to conclude that the "volatile factor" is, undoubtedly, water.

Table 1. Effectiveness of water and other substances in promoting insect spermatocyte differentiation in large culture chambers.

Cultures with active blood and cysts (No.)	Conditions	Drops of other liquid (No.)	Experiments (No.)	Cysts developed at 5 days (%)
	Series 1a. Development of cysts in a single drop of active blood			
1	Sealed depression slide		14	42
	*Series 1b. Development of cysts in active blood in the presence of other active cultures**			
1			6	0
2			4	4
4			4	13
6			2	42
8			3	35
12			2	45
16			2	52
	*Series 1c. Development of cysts in active blood in the presence of water**			
1		0	2	0
1		1	2	7
1		3	7	11
1		5	2	44
1		7	7	56
1		9	2	54
1		11	2	54
1		13	2	40
1		15	7	58
	*Series 2. Development of cysts in active blood in the presence of complete and incomplete cultures**			
1	Active blood and cysts	15	3	42
1	Inactive blood, no cysts	15	4	41
1	Active blood, no cysts	15	3	42
1	Inactive blood and cysts	15	2	46
	Series 3. Differentiation of cysts in active blood in the presence or absence of sufficient quantities of water†			
1	No water supplement		4	0
1	Water supplement (5 ml)		4	45
	Series 4. Development of cysts in the presence of increasing numbers of active cultures, with an excess of water			
1	Depression slide		3	35
1	Water (5 ml)*		4	36
2	Water (5 ml)*		2	33
4	Water (5 ml)*		2	45
8	Water (5 ml)*		1	36
16	Water (16 drops)*		2	35
	*Series 5a. Development of cysts in active blood in the presence of silica gel (0.1 to 0.2 g)**			
4	Dehydrated SiO_2		2	6
8	Dehydrated SiO_2		2	9
4	Hydrated SiO_2		2	20
8	Hydrated SiO_2		2	41
	*Series 5b. Development of cysts in active blood in the presence of copper sulfate (0.1 to 0.2 g)**			
4	Dehydrated $CuSO_4$		2	0
8	Dehydrated $CuSO_4$		2	0
4	Hydrated $CuSO_4$		2	23
8	Hydrated $CuSO_4$		2	37

* In a 60-mm petri dish (volume about 30 cm^3). † In a 100-mm petri dish (volume about 100 cm^3).

To summarize, a reinvestigation of the "volatile factor" proposed by Ketchel and Williams (*1*) was carried out, a number of their experiments being repeated under presumably identical conditions. One exception to the complete uniformity was that blood and cysts used here were derived from *Samia cynthia*, a species closely related to *Hyalophora* (*Samia*) *cecropia*. This difference of material could not have affected the results, since Schmidt and Williams (*4*) have reported that *H. cecropia* and *S. cynthia* blood and germinal cysts behave identically in culture to the extent that the cysts of each species can differentiate in the blood of the other. Despite the several similarities of experimental results, our study indicates that the "volatile factor" is

As additional confirmation the effects of desiccants were assessed. Culture dishes with sufficient numbers of active drops to permit maximal development were compared with similar dishes to which the desiccant was added. The additive was either indicating silica gel (mesh size, 6–16), which is capable of absorbing more than 40 percent of its weight in water, or copper sulfate. Control cultures contained 0.1 to 0.2 g of the water-saturated desiccant, while the experimental cultures were given the same material after it had been dried in heat.

The cultures with dry desiccant produced a lower percentage of developing cysts than those with the saturated reagent (Table 1, ser. 5). While we do not know whether silica gel or copper sulfate absorbs compounds in addition to water, they should differ in this respect. It should be pointed out that Ketchel and Williams attempted unsuccessfully to absorb the "volatile factor" with Ringer's solution, dilute alkali, and acid. They were partially successful with activated charcoal and, possibly, with mineral oil. The major constituent absorbed by silica gel and copper sulfate is water. It appears that the addition of small amounts of active desiccant to the cultures lowered the percentage of cyst differentiation, an effect not produced by water-saturated desiccants.

water. No other interpretation appears possible.

This interpretation explains not only all of our results but also some results of the earlier workers which heretofore have not been adequately explained. To cite just one example, the observation that the differentiation of cysts in 16 drops of active blood was greatly enhanced above the value obtained for the same number of cysts in two drops can be interpreted as simply a consequence of the larger amount of water available (*5*).

HANS LAUFER
RONALD H. BERMAN
Department of Biology,
Johns Hopkins University,
Baltimore, Maryland

References and Notes

1. M. M. Ketchel and C. M. Williams, *Biol. Bull.* **109**, 64 (1955).
2. H. A. Schneiderman, M. M. Ketchel, C. M. Williams, *ibid.* **105**, 188 (1953).
3. H. Laufer, *Ann. N.Y. Acad. Sci.* **89**, 490 (1960).
4. E. L. Schmidt and C. M. Williams, *Biol. Bull.* **105**, 174 (1954).
5. This work was supported in part by the National Science Foundation (grant No. G9833). Dr. Laufer was a fellow of the National Research Council from 1957 to 1959, at the Department of Embryology, Carnegie Institution of Washington, Baltimore, Md.; Mr. Berman's work was supported in part by an undergraduate biological research award (G3383) from the National Science Foundation.

1 August 1960

Punishment in the Squirrel Monkey Saimiri sciurea

Abstract. Punishment has been found not only to suppress the rate of a food-maintained operant response in the squirrel monkey under conditions of high deprivation but to inhibit the emission of that response for 50 days (400 hours) after the punishment has been withdrawn.

Since the publication of Estes's "An Experimental Study of Punishment" (*1*), the effects of presenting a severely aversive stimulus, such as a strong electric shock, contingent upon the emission of a response have been generally regarded as temporary. When shocks were of such an intensity as to completely suppress the rate of bar-pressing in the rat, Estes found that recovery occurred when the punishing stimulus was withdrawn. Recently, Azrin (*2*) found that during prolonged exposure to punishment the rate of a pigeon's key-pecking in the presence of shock returned to a level comparable to that observed before the introduction of punishment. In pigeons subjected to very severe current intensities, however, Azrin (*3*) reported recovery only about 12 days after the shock had been removed.

Little is known about the effects of punishment on the behavior of higher organisms, such as the monkey, although a considerable amount of research on a related phenomenon, conditioned suppression, has been reported, most recently by Brady (*4*) and Sidman (*5*). In this experiment I used a technique similar to that of Azrin, with squirrel monkeys as subjects, in an attempt to extend the earlier findings to a wider variety of species (*6*).

Two experimentally naive, adult, short-haired squirrel monkeys (*Saimiri sciurea*) were starved to 80 percent of the body weights they had had on a free-feeding regimen and were then conditioned to press a lever for food rewards. During the initial stages of training every response was reinforced; later, responding was reinforced intermittently, with mean intervals of first 1, then 3, and finally, 6 minutes between rewards (VI-1, VI-3, and VI-6). After the rate of response had been stabilized on the VI-6 schedule, the experiment was begun. Table 1 summarizes the procedures and results.

Each daily session lasted for 8 hours, so that, although the number of animals available was small, a considerable amount of data were gathered (560 hours for each monkey). On days 1 to 7 the subjects were run on the VI-6 schedule; no punishments were given. During this period an average of 2846 responses were made each day by monkey No. 19 and 2246 by monkey No. 20.

On day 8 the punishment procedure was instituted. After each response, an electric shock of 1-ma intensity and 500-msec duration was given through a grid floor, through the walls of the box in which the monkeys were run, and through the lever. The number of responses in 8 hours was 65 for monkey No. 19 and 29 for monkey No. 20. During the next 11 days the same procedure was in effect, and the number of responses fell to an average of nearly one per day for both animals. This means that the monkeys obtained virtually no food for 8 hours; their weights therefore declined rapidly (as mentioned above, the monkeys were at 80 percent of their normal weights before the experiment began). The weights were allowed to fall an additional 100 g (to 60 percent of normal) before the animals were given food in their home cages, to prevent death and in order to continue the experiment. Punishment was withdrawn on the 20th day, and during succeeding sessions the mean interval between reinforcements was decreased. There was no recovery in the rate of response during the next 50 days (400 hours); then the experiment was terminated.

The monkeys, after punishment was instituted, and thereafter, showed an unwillingness to enter the experimental chamber and what could probably be described as "fearful" behavior when they were finally placed in the box. They would crouch in the corner farthest from the lever and would remain there during the entire session. This behavior persisted throughout the 50 days from the termination of punishment until the end of the experiment.

Table 1. Summary of procedures and results. CRF, every response reinforced.

Schedule of reinforcement	Punishment condition	Mean No. of responses per session	
		Monkey No. 19	Monkey No. 20
	Days 1–7		
VI-6	Off	2846	2246
	Day 8		
VI-6	On	65	29
	Days 9–19		
VI-6	On	1.4	0.9
	Day 20		
VI-6	Off	0	0
	Days 21–34		
VI-1	Off	1.3	0
	Days 35–55		
VI-½	Off	0.8	0.6
	Days 56–70		
CRF	Off	1	0.9

It would appear that the squirrel monkey does not recover from the effects of punishment as do the pigeon and the rat. However, this is not certain, since there were differences other than that of species between the conditions of the study reported here and conditions of the studies of Estes and Azrin—for example, differences in shock intensity and duration, method of presentation of shock, and frequency of food reinforcement. It does, however, seem reasonable to suppose that the monkey may be more sensitive than the pigeon and may therefore be more like man. If this is correct (and further research is needed before any definite conclusions are drawn), severe punishment may have the effect not only of eliminating any desired response but also of permanently inhibiting adaptive behavior in higher organisms.

JAMES B. APPEL*
Indiana University Medical Center,
Indianapolis

References and Notes

1. W. K. Estes, "An Experimental Study of Punishment," *Psychol. Monographs, No. 263* (1944).
2. N. H. Azrin, *Science* **131**, 605 (1960).
3. ———, *J. Expt. Anal. Behavior* **3**, 123 (1960).
4. J. V. Brady, *Proc. Assoc. Research Nervous Mental Disease* **37**, 104 (1959).
5. M. Sidman, *Science* **132**, 61 (1960).
6. I wish to thank C. B. Ferster for providing facilities for this research.
* Present address: Yale University School of Medicine, New Haven, Conn.

10 October 1960

Behavioral Method for Study of Pain in the Monkey

Abstract. A behavioral method is described in which increasing intensities of electric shocks were applied to the gasserian ganglia of alert monkeys. The animals were trained to press a lever to regulate the shock level. "Pain thresholds" were thereby obtained, and these thresholds were modified by varying the shock duration and by administration of morphine.

The need for quantitative measures of pain threshold in alert, active animals prompted development of the following technique. It resembles the methods used to measure auditory threshold responses in man (*1*) and sensitivity to foot shock in rats (*2*). In two rhesus monkeys the gasserian ganglion was implanted under surgical anesthesia with bipolar stainless steel electrodes, each consisting of two insulated 0.010-inch-diameter wires twisted together with insulation removed for only 1 to 2 mm at their tips. This implantation was accomplished in one case under direct visual control and in the other by predetermined Horsley-Clarke coordinates. The electrodes were fixed to a Sheatz (*3*) pedestal to which a connecting cable could be attached for delivery of electric shocks to the ganglion.

Several days postoperatively, stimulation consisting of a train of three negative square waves, each separated by 32 msec, was applied to the ganglion every second. The duration of each square wave was varied between 0.005 and 1 msec in different experimental sessions. The intensity (voltage) of the stimulus was controlled by a stepping relay that automatically raised it one step (approximately 0.75 volt) every 5 seconds. The maximum intensity reached through 25 steps was 18.5 volts (*4*).

Both monkeys were trained in this postoperative phase to press a microswitch lever; each press resulted in the reduction of the intensity of the shock by one step (approximately 0.75 volt). Thus each animal came to have complete control of the level of the aversive stimulus and by pressing rapidly could quickly decrease the shock intensity to zero.

The animals were maintained for several weeks of such experimentation in the primate chair described by Mason (*5*) located in an acoustically insulated booth with a one-way window. In one monkey a No. 90 polyethylene catheter was permanently placed into the right atrium by way of the right jugular vein, led subcutaneously to the occipital region and fixed to the skull in a modified Sheatz pedestal. This catheter, extended by similar tubing to the outside of the booth, was used for introducing drugs into the circulatory system without disturbing the animal.

Two methods were used to record the animal's lever-press response. Automatic counters recorded both the number of times the stepping relay was at each intensity and the number of times the animal responded at each intensity; additionally, a Varian G-10 recorder presented a continuous graphic recording of the level of shock intensity maintained.

In the experimental sessions both animals maintained a definite level of tolerated shock intensity. With a fixed square-wave duration this level usually remained quite constant over a 6-to-8 hour test period for a particular day and from one day to the next. However, occasionally a gradual rise of level of approximately 25 percent was observed. When voltage and current were simultaneously monitored, an increase of approximately 25 percent in tissue resistance was also found during the same period.

The behavioral level could be raised or lowered by changing the duration of the square-wave pulses applied. For square-wave durations above 0.7 msec the animal would maintain the shock intensity between step 0 and step 2. For all durations below 0.01 msec the level maintained was between steps 15 and 25. When the shock was turned off, the animals usually stopped lever pressing, but occasionally continued responding for several minutes. Such factors as hunger, the presence of the experimenter, and a previous strong shock to the ganglion would change the tolerated level to a significant degree; occasional marked changes in threshold from day to day remain unexplained.

Since at certain stimulus levels contractions of the facial muscles occurred, the question arose as to whether some afferent input other than pain was controlling the lever-pressing behavior. Morphine was therefore administered to test whether the maintained level represented a "pain tolerance threshold." Three doses (0.125, 0.25, and 0.50 mg/kg) were given through the indwelling catheter. At least 3 days separated each dose. None of the doses induced lethargy or somnolence, and whenever the experimenter directly confronted the drugged monkey the animal behaved in an apparently normal manner.

The level of shock tolerated rose

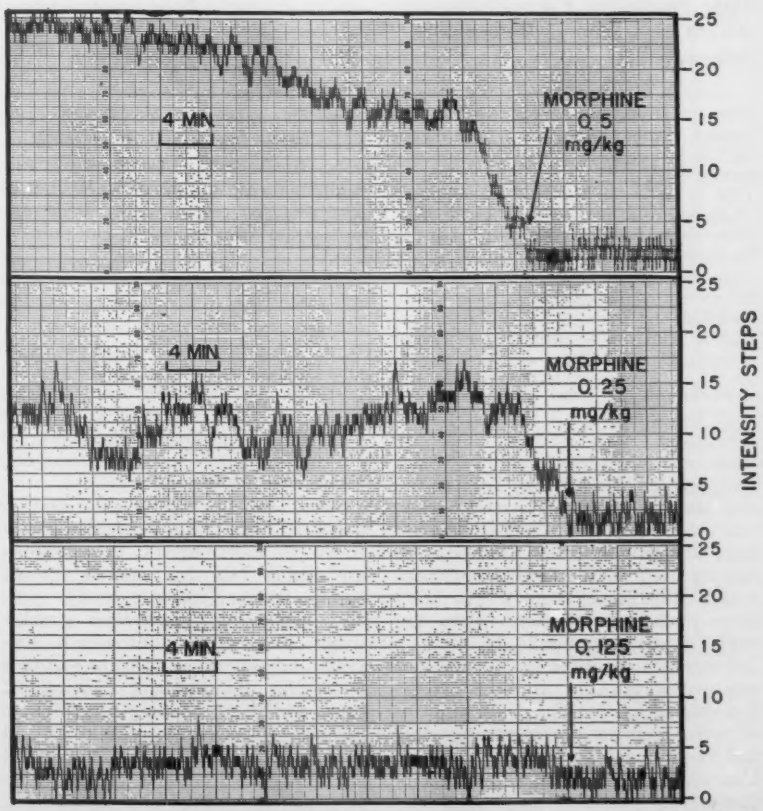


Fig. 1. Effect of intravenously administered morphine sulfate (0.125, 0.25, and 0.50 mg/kg) on threshold levels. Records read from right to left.

under the influence of the drug in proportion to the dose administered (see Fig. 1). The duration of the effect similarly was correlated with the dose level. The fact that the behavioral response is sensitive to the well-known analgesic property of morphine strongly suggests that the afferent inflow controlling the lever pressing is related to pain. The method described would therefore appear to provide a useful tool for further investigations of pain perception.

ELLIOT D. WEITZMAN,
GILBERT S. ROSS,
WILLIAM HODOS, ROBERT GALAMBOS
Departments of Neurophysiology and Experimental Psychology, Walter Reed Army Institute of Research, Washington, D.C.

References and Notes

1. G. von Békésy, *Acta Oto-Laryngol.* **35**, 411 (1948).
2. B. Weiss and V. G. Laties, *Science* **128**, 1575 (1958).
3. G. C. Sheatz, in *Houston Symposium on Brain Stimulation Subcortical Systems* (Univ. of Texas Press, Austin, in press).
4. We are indebted to Dr. Murray Sidman for valuable suggestions on designing the apparatus.
5. J. W. Mason, *J. Appl. Physiol.* **12**, 130 (1958).

13 October 1960

Early Pleistocene Paleoclimatic Record from Sonoran Desert, Arizona

Abstract. Three pollen spectra from lake sediments stratigraphically well below mid-Kansan fauna indicate plant associations for the Sonoran desert, Arizona, approximating those found now at elevations of 1500 ft and more above the desert floor. The presence of *Ostrya, Betula,* and *Artemisia* may indicate some invasion by northern species as well. A climate cooler or wetter, or both cooler and wetter, than the present climate is inferred from paleobotanical and sedimentary evidence. Correlation with the Nebraskan glacial stage is tentatively suggested.

A durable problem of paleoecology and biogeography is the effect of Pleistocene climatic fluctuations on biota of nonglaciated regions. Since this problem relates to vegetational changes, it is unlikely that any method will prove more fruitful for its solution than stratigraphic pollen analysis. Pioneering attempts to establish continuous pollen chronologies in the southwestern states have been made by Clisby and Sears (*1*) and by Roosma (*2*).

Sediments deposited in pluvial lakes that existed through part or all of the Pleistocene in the Far West are invaluable archives of lithostratigraphic and vegetational history. According to Lance (*3*), late Cenozoic [Pliocene (?)–Pleistocene] lacustrine and alluvial sediments accumulated to unknown depths in the northwest-trending structural trough of the Safford-San Simon valleys, Graham County, southeast Arizona, until nearly the middle Pleistocene. Down-cutting and degradation then became dominant processes following drainage of ponded water in the valleys. The Gila and San Simon rivers now have trenched middle and early Pleistocene sediments flooring and underlying the valleys, exposing them for several hundred feet. At several localities these sediments contain Blancan fauna (*4*). Vertebrate fossils considered transitional Blancan to Irvingtonian, or of approximate middle-Kansan age in terms of North American glacial chronology, are encountered in lacustrine-paludal sediments near the top of the exposed Pleistocene sequence (*5*) and 400 to 600 ft stratigraphically above the pollen-bearing sediments of the valley floor.

Shallow drill holes in the valley floor made during exploration for watershed dam sites (*6*) yielded core sediments that were exhaustively sampled for pollen. Well-preserved, abundant grains were obtained from only one core (Table 1, columns 2 and 3). Some core cuttings (*6*) (Table 1, column 1) also contained pollen, although sediments from outcrops were mostly barren. Sufficient stratigraphic control to clearly relate the column 1 spectrum to the others is lacking. Topographic relations suggest that this pollen horizon is higher in the lake-bed sequence than the pollen horizon from the 43- to 48-ft levels.

These single records provide rare evidence of the nature of early Pleistocene climate in the Southwest. Because additional data for the area may not be available for several years, these records seem worthy of present publication.

Elevations approximate 3000 to 3200 ft where the Safford Valley borders the Pinaleno Mountains (about 10,700 ft) to the southwest and the Peloncillo and Gila ranges (about 7000 ft) to the northeast. No available evidence suggests that these topographic relations were not stable during deposition of Pleistocene and Pliocene (?) sediments underlying the valley.

Mean annual, biseasonal rainfall is about 10 inches and is largely concentrated as short, intense thundershowers during July and August. Desert shrub—*Larrea* (creosote bush), *Atriplex* (saltbush), *Gutierrezia* (snakeweed), *Haplopappus* (burroweed), *Prosopis* (mesquite), *Ephedra*—scatters the valley floor. Major vegetational zones in the surrounding foothills and uplands, with increasing rainfall and decreasing temperatures, include desert grassland (3500 to 4800 ft), oak (juniper-pine) woodland (4800 to 6500 ft), ponderosa pine (6500 to 8000 ft), and Douglas fir–white fir (8000 ft and above) (*7*). Pollen, borne into Safford Valley by wind or water, or by both, is shown by analysis of contemporary sediments (Table 1, columns 4 and 5).

The generally high percentages (Table 1, columns 1 to 3) of juniper, sagebrush, pine, and oak indicate a marked departure for early Pleistocene vegetation from the prevailing lower Sonoran flora of Safford Valley. These genera apparently invaded the sclerophyllous shrub and desert grassland of the lower valley and upper desert slopes, while mesophilous trees and shrubs [walnut, hackberry, sycamore (?), ash] clustered in nearby draws on flood plains of streams and possibly at the lake margin. The base of the sequence (43 to 48 ft) suggests an open savanna-parkland [juniper–oak–pine–(shrubby [?] sagebrush)] with intervening grasses and some forbs and perennial shrubs typical of lower slopes and valley floor. Woodland assumed increased importance in the uppermost horizon with pine a dominant at low elevations though probably above the lake margin (*8*). The pollen of several boreal and subalpine genera [alder, birch, Douglas-fir (?), fir, hop hornbeam, maple, spruce] evidently sifted to the lowlands from forests well above the valley. The limited but consistent occurrence of several of these pollen types supports other floral evidence favoring depression of vegetational zones in this area during the early Pleistocene.

The finding of elm pollen provides a range extension for a genus no longer indigenous to the Southwest; at least two northern Arizona species (hop hornbeam, birch) reached this latitude in the early Pleistocene. High percentages of sagebrush pollen may indicate immigration of a northern shrubby *Artemisia* into southeastern Arizona lowlands, although it seems possible that increased abundance of a local herbaceous species, under altered climatic conditions, might account for the high frequency of sage pollen in these sediments (*9*). Pure stands and high concentrations of the most conspicuous of the shrubby artemisias, *A. tridentata*, do not now occur south of the Mogollon Rim, at elevations below 5000 ft. The herbaceous *A. dracunculoides* and *A. ludoviciana*, though readily overlooked in the field, are common though somewhat local members of southeastern Arizona vegetation at low and moderate elevations (*10*). Fletcher (*11*) indicates the root perennial *A. carruthii* to be widespread and common in the bordering foothills and adjacent uplands (3500 to 8000 ft) of the Pinaleno Mountains, although it does not occur in high concentrations. According to Fletcher and Goodding, this species may flower in both spring and fall. A possible biseasonal anthe-

sis, combined with profuse flowering and large amounts of pollen shed, make this species a potentially important factor in the pollen rain. Nevertheless, the limited quantity of sage pollen now encountered in contemporary southern Arizona sediments (*12*) provides a paradox which makes the high percentages of *Artemisia* pollen in the Safford Pleistocene spectra inexplicable in terms of the distribution and frequency of herbaceous species now inhabiting the area.

A climate at least temporarily cooler and probably wetter than the climate today is indicated for early Pleistocene southeast Arizona. The apparent shift in valley vegetation from open mixed parkland to more closed (?) pine woodland stresses the climatic alteration. K. Clisby suggests, further, the possible significance of the inverse ratio between tree pollen plus sage and chenopods in fossil and contemporary spectra in underlining moist-to-dry climatic change. The climate projected from pollen analysis is corroborated by past lacustrine conditions in the Safford–San Simon valleys. The lake beds are on the order of 2000 ft thick and extend over an area of at least 35 miles; water-level changes within them, inferred from sedimentary evidence, suggest climatic oscillations possibly of interstadial magnitude (*13*). Equatorward shift of the Pacific winter cyclonic storm track, now scarcely extending into Arizona, is postulated to explain atmospheric conditions requisite for lake expansion in now arid-semiarid middle latitudes during times of glaciation to the north (*14*). Thus it seems probable that winter rains played a more significant role than they do currently in the predominantly summer-shower region of southeastern Arizona. The abundance of sagebrush may suggest a pluvial phase shift in the seasonal precipitation pattern.

From (i) the stratigraphic position, (ii) the presence of a "cool" flora, and (iii) the availability of a large, possibly deep, lake as deposition site, it seems probable that the Safford spectra register climate within some phase of the Nebraskan glacial stage. Or, they may indicate a pre-Nebraskan cooling corresponding to the Donau stage of the recognized European glacial sequence. More knowledge about past rates of regional sedimentation and additional stratigraphic and paleobotanical control are necessary, however, for more exact correlation with glacial events of the early Pleistocene (*15*).

JANE GRAY

Geochronology Laboratories, University of Arizona, Tucson

Table 1. Percentage frequency of pollen and spores in early Pleistocene (columns 1–3) and contemporary (columns 4, 5) sediments of the Safford-San Simon valleys. Depth is depth below the surface. Figures in parentheses are number of grains.

Group, family, or genus	*1* Kennecott core (depth, 257–272 ft; *N*, 1642; el., about 3300 ft)	*2* Safford core (el., 2995 ft) Depth, 43.5 ft; *N*, 1108	*3* Safford core (el., 2995 ft) Depth, 48.0 ft; *N*, 1137	*4* Gila River mud (*N*, 715; el., 2930 ft)	*5* 111 Ranch water storage tank (*N*, 962; el., 3400 ft)
Juniperus-Cupressus	4.2	15.7	26.9	2.9*	0.4 (4)
Quercus	3.5	11.4	6.7	3.9	0.6 (6)
Pinus	52.6	5.0	10.6	3.0	1.4
Artemisia	11.0	13.5	13.5		0.1 (1)
Compositae (other)	4.0	22.8	14.4	34.8	20.5
Liguliflorae	0.06 (1)	†	0.1 (1)		
Gramineae	9.5	11.3	6.2	3.2	9.0
Chenopodiaceae–					
Amaranthus	6.3	6.3	9.9	38.9	41.7
Sarcobatus	3.6		0.5 (6)		
Tidestroemia	0.06	0.1 (1)	0.4 (4)	0.3 (2)	
Abies	0.43 (7)	0.2 (2)	0.3 (3)		
Acer (see *A. negundo*)			†		
Acacia	† (?)		†	0.3	0.6
Alnus	0.12 (2)		0.2 (2)		
Betula	0.12				
Celtis		0.4 (4)			0.1
Cereus-type					0.1
Ephedra spp.	0.36 (6)	†	0.1	2.0	0.7 (7)
Ericaceae					0.1
Fraxinus	0.06	0.3 (3)	0.6 (7)		
Garrya	†		†		0.1
Juglans	0.18 (3)	0.6 (7)	0.3	0.1	
Opuntia				0.1 (1)	
Ostrya	0.24 (4)	1.5	0.3		
Picea		0.1	0.2		
Platanus (?)			0.4 (5)		
Prosopis					10.2
Pseudotsuga (?)	0.12				
Salix (?)	0.06				
Ulmus	0.06	0.3	0.1		
Vitis			0.1		
Cyperaceae	0.49 (8)	1.4	0.6		
Epilobium-type	0.06	0.1			0.2
Eriogonum aureum-type	0.06		0.1	0.3	0.2
E. albertianum-type					1.2
Erodium					0.1
Euphorbiaceae					0.2 (2)
Gilia-type	†	0.1	0.1	0.1	0.2
Liliaceae					0.2
Linanthus-type			†		
Nyctaginaceae			†	0.6 (4)	0.3
Plantago	0.06				
Sphaeralcea-type	0.06	0.1	†	1.7	2.1
Thalictrum	0.06				
Typha angustifolia	1.0	0.6	0.2		
Polypodiaceae (?) (monolete, trilete spores)	0.06		†	†	0.1
Selaginella		†	†	†	
Pediastrum	†	†	†		
Botryococcus	†		†		
Unidentified pollen	1.6	8.2	7.2	7.4	9.5

* Higher percentages of juniper, oak, and pine in the river mud than in storage-tank *gyttja* may indicate limited water transport of these grains from the upper reaches of the Gila River in the Gila Range. † Scanned.

References and Notes

1. K. H. Clisby and P. B. Sears, *Science* **124**, 537 (1956).
2. A. Roosma, *ibid.* **128**, 716 (1958).
3. J. F. Lance, personal communication.
4. M. M. Knechtel, *Am. J. Sci.* **31**, 81 (1936).
5. J. F. Lance, *Bull. Geol. Soc. Am.* **69**, 1693 (1958).
6. The cores were supplied by W. Mindter; cuttings were provided by E. Davidson through the courtesy of Kennecott Corp.
7. W. P. Martin and J. E. Fletcher, *Univ. Ariz. Tech. Bull. No. 99* (1943).
8. Size-frequency studies of pine, spectra 1 and 3, indicate distinctly larger grains for spectrum 1, although both populations fall within size-range variations of *Pinus cembroides* (pinyon). The larger size-range variation and bimodal curve of spectrum 1 population may indicate that it embraces more than one species.
9. *Artemisia* pollen species are not readily distinguished; morphological variation among fossil grains suggests the presence of more than one species.
10. C. Mason and L. N. Goodding, personal communication.
11. J. F. Fletcher, personal communication.
12. J. Gray, unpublished analyses. In Huachuca Canyon (5840 ft) contemporary sediments contained only 1.95 percent of sagebrush pollen (high for southern Arizona), although Goodding tells me *Artemisia* is very abundant there.
13. J. Harbour, personal communication.
14. R. F. Flint, *Glacial and Pleistocene Geology* (Wiley, New York, 1957).
15. This report is contribution No. 41 of the University of Arizona's program in geochronology; the research was supported by the Rockefeller Foundation through the university's "Utilization of Arid Lands" program.

31 October 1960

Alteration of Mutation Frequency by Treatment with Actinomycin D

Abstract. The frequency of lethal mutations occurring in *Drosophila melanogaster* was reduced by approximately one-half when irradiated males were treated with actinomycin D, which also inhibited the appearance of melanotic atypical growths in the strain used for the study.

In the course of investigations on alteration of mutations, actinomycin D was administered to a strain of *Drosophila* developing tumors, and mutation frequency and tumor incidence were determined after irradiation. The *st sr e^s ro ca; tu 36^a* strain, which has an unusually constant but low incidence of tumors due to multiple recessive genes, was used in these studies. Preliminary tests on sex ratios in individual matings were used to reduce the likelihood of antecedent lethal mutations. One-half of the males raised on medium containing antibiotic in 1×10^{-3}-percent concentration were irradiated with 3000 r [6 ma, 100 kv (peak), 1.0 mm of Al, 15 cm] at the age of 3 days. The *sc^{81} B InS w^a sc^s* inversion and sequential matings of the Muller 5 type were utilized to detect lethal mutations on the X chromosome (Table 1). Semilethals and visibles are not included in the tabulations. Determinations of tumor incidence in P_2 and F_1 generations (*1*) were also recorded and are presented in Tables 2 and 3. Untreated cultures and cultures treated with actinomycin D alone and irradiation alone were also studied in a similar manner.

Table 1. Effect of actinomycin D on mutation rate in *Drosophila*.

Treatment	Chromosomes tested	Lethal mutations	
	(No.)	No.	%
Control	1375	2	0.14
Actinomycin D	978	1	0.10
Irradiation (3000 r)	1168	67	5.73
Irradiation (3000 r) plus actinomycin D	952	31	3.25

The usual frequency of mutation was found in the control cultures (two lethals among 1375 chromosomes tested), and no significant difference was encountered when actinomycin D was added to the medium. However, the frequency with irradiation, 5.73 percent, was reduced to 3.25 percent when actinomycin D was present in irradiated cultures. In the P_2 generation, any tumors formed had regressed, leaving a pigmented residue before irradiation, so that no difference was expected between irradiated and nonirradiated cultures. The presence of actinomycin D resulted in significant reduction ($p < .05$) in tumor incidence in each group, however. In the F_1 generation, the antibiotic alone and irradiation alone reduced the number of tumors as compared to the control group. Irradiation did not reduce the number of tumors by a significant additional amount when used as a supplement to treatment with actinomycin D.

The current studies show a reduction in the number of atypical growths in *Drosophila* after treatment with actinomycin D, but inhibition of tumors by both the antibiotic and irradiation suggests that in neither case is this effect mediated through the mechanism of mutation. Actinomycin D undoubtedly reduces the number of lethal mutations occurring after x-irradiation ($p < .05$). Whether a similar reduction in the frequency of natural mutations can be demonstrated by extending the scope of the tests remains to be seen. Although the mechanism (*2*) is obscure at present, the implications of the effective reduction of irradiation-induced mutation in metazoa by an agent which can be administered in therapeutic dosage would seem of some interest (*3*).

WALTER J. BURDETTE

Department of Surgery and *Laboratory of Clinical Biology, University of Utah College of Medicine, Salt Lake City*

Table 2. Effect of actinomycin D on incidence of tumors in *Drosophila*.

Treatment	Males			Females			Total		
	Tumors	Total	%	Tumors	Total	%	Tumors	Total	%
Control	133	1644	8.1	127	1520	8.4	260	3164	8.2
Actinomycin D	20	514	3.9	24	493	4.9	44	1007	4.4
Irradiation (3000 r)	88	971	9.1	79	1069	7.4	167	2040	8.2
Irradiation (3000 r) plus actinomycin D	22	502	4.4	11	505	2.3	33	1007	3.3

Table 3. Effect of actinomycin D and irradiation on incidence of tumors in *Drosophila*.

Treatment	Males			Females			Total		
	Tumors	Total	%	Tumors	Total	%	Tumors	Total	%
Control	387	6110	6.3	378	6217	5.38	765	12357	6.2
Actinomycin D	34	1762	1.9	34	1731	1.96	68	3593	1.9
Irradiation (3000 r)	119	4474	2.7	145	4416	3.24	264	8890	3.0
Irradiation (3000 r) plus actinomycin D	29	1113	2.6	20	1115	1.79	49	2228	2.2

References and Notes

1. W. J. Burdette, *Cancer Research* **11**, 552 (1951).
2. L. S. Altenburg, *Proc. Natl. Acad. Sci. U.S.* **40**, 1037 (1954); T. Chang, F. D. Wilson, W. S. Stone, *ibid.* **45**, 1397 (1959); F. H. Dickey, G. H. Cleland, C. Lotz, *ibid.* **35**, 581 (1949); A. Hollaender, D. Billen, C. O. Doudney, *Radiation Research* **3**, 235 (1955); V. J. Horgan and J. S. Philpot, *Radioblol. Symposium, Proc., Liège, 1954* (1955); R. F. Kimball, N. Gaither, S. M. Wilson, *Radiation Research* **7**, 490 (1959); R. Latarjet, *Ciba Foundation Symposium. Ionizing Radiation and Cell Metabolism, 1956* (1957); W. L. Russell, L. B. Russell, E. M. Kelly, *Science* **127**, 1546 (1958); G. Scholes and J. Weiss, *Radiation Research, Suppl.* **1**, 177 (1959); G. Scholes, J. Weiss, C. M. Wheeler, *Nature* **178**, 157 (1956); F. H. Sobels, *Intern. J. Radiation Biol.* **2**, 68 (1960); W. S. Stone, O. Wyss, F. Haas, *Proc. Natl. Acad. Sci. U.S.* **33**, 59 (1947); M. Westergaard, *Experientia* **13**, 224 (1957).
3. This work was aided by a grant from the U.S. Public Health Service, Department of Health, Education, and Welfare.

29 August 1960

Modification of Cortically Induced Responses in Brain Stem by Shift of Attention in Monkeys

Abstract. The long-latency electrical response of the brain stem evoked by stimulation of the cortex of freely moving monkeys is modified by a change of attention. The modification may be either suppression or augmentation, according to the background activity prior to the shift of attention.

In conscious cats the size of sensory evoked potentials is modified as far down as second-order sensory neurons according to the state of attentiveness of the animal (*1*). This phenomenon is interpreted as due to inhibitory influences descending through the reticular core. While it is obvious that the focusing of attention requires a selective facilitation of certain sensory input above other sensory afferents, it is not clear whether a similar mechanism applies to the situation where a corticifugal impulse is interacting with sensory afferents, or vice versa.

In this study of the central biological action of urine extracts from schizophrenic subjects (*2*), a number of *Macaca* monkeys with a system of 42 to 50 permanently implanted electrodes were used (*3*). In these animals which were kept from over 6 months to 2

years, it has been possible to correlate certain electrophysiological phenomena with behavioral changes.

Two sets of cortically induced long-latency responses in the brain stem were observed. Recording was made through the Teflon–coated bipolar electrode (No. 36 platinum iridium wires) separated 0.5 mm at the tip. One such response was recorded in the subthalamus after stimulation of the sensorimotor cortex in two monkeys, and the other was recorded in the nucleus of the third nerve after stimulation of the parietal cortex in three monkeys. All recording sites have been verified histologically. Stimuli up to 10 volts at 200 pulses per second (pulse duration, 0.1 msec) applied to the subthalamus did not produce any overt behavior except for brief facilitation of sensory evoked potentials in the diencephalic structures following such tetanization. Stimulation of the posteriorly placed, midline electrode in the nucleus of the third nerve produced an elevation of the upper eyelids and an inward rotation of the eyeballs (Fig. 1*B*).

The cortical stimuli were square wave pulses of 6 to 8 v and 0.1 msec duration, applied at a rate of 1 to 2 pulses per second. The animals did not show any overt behavioral change. Only when the intensity of the stimulus was sufficiently raised did the animal lift its contralateral hand as if some sensation were referred to it.

Although the recording and stimulating loci were different in these animals, it was found that the size, shape, and behavior of these evoked potentials were extremely similar. Both responses were characterized by a large negative potential with the latency of its peak about 100 msec and of 200 to 250 msec duration (Fig. 1*C*). This response was most conspicuous when the animal was relaxed, and its amplitude became largest when the animal was drowsy. In the latter case this negative wave was followed by a rather prominent positivity. As long as the animal was relaxed, the amplitude of the response remained consistently high, although it showed a definite tendency to wax and wane. Such waxing and waning were not correlated with any recognizable change of gross electrographic patterns from a number of cortical and deep structures so far investigated.

The brain stem response was significantly depressed when the animal became alert, or it practically disappeared. When the animal looked at its own hand, probably because of an induced paresthesia from stimulation of the sensory cortex, the response was suppressed. Such a modification of the response was also evident when a novel stimulus, such as a click or a flash of light, was introduced or the amount of room light was suddenly changed. However, as the animal gradually adapted to a new situation the amplitude of the response returned to normal (Fig. 1*D*).

So far the most powerful suppressor of such brain stem response has been the visualization of laboratory workers (Fig. 1*A*). When the animal discovered that it was being watched, the response was depressed as long as the animal could see the experimenter through the one-way mirror. Although the animal carefully followed every minor move of the experimenter with its gaze, such an obvious alertness on the part of the animal was not always accompanied by a flattening of the response. However, such flattening regularly occurred whenever the animal realized that the experimenter's gaze was fixed on it. This specific nature of the most powerful suppressor of the response—that is, the direct meeting of the experimenter's gaze and that of the monkey—suggests concentrated focusing of discriminatory attention of a quality necessary for self-preservation in the monkey. Since three recording sites of the response, which fluctuated according to the animal's state of attentiveness, were located in or around the nucleus of the third nerve, and since focusing of attention is usually accompanied by a shift of gaze, eye movement itself as a source of cortical-response modification cannot be ruled out, although it is an unlikely one.

Sometimes the reduction or flattening of the response was found to last for a considerable period of time even though there was no recognizable environmental change in a quiet animal chamber. On such occasions the animal was usually showing a facial expression of "preoccupied relaxation." Whether such a sustained flattening of the response is due to the animal's attention to the effect of cortical stimulation or whether it is due to some unknown change in *milieu intérieur* is not clear.

However, it was under such circumstances that a novel afferent sensory

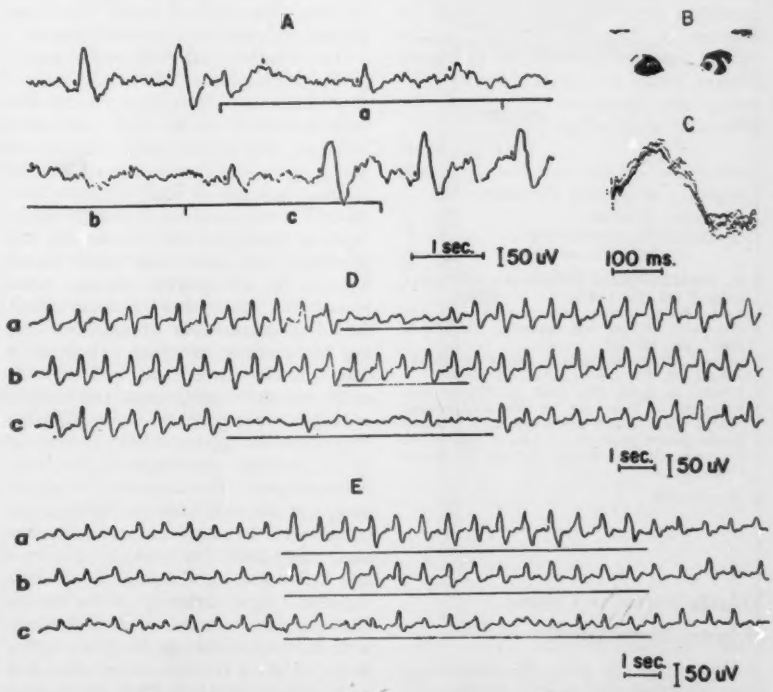


Fig. 1. Electroencephalographic records of two monkeys. *A* and *B*, monkey "Shiro"; *C*, *D*, and *E*, monkey "Goro." (*A*) The records are continuous. The short vertical marks indicate cortical (parietal) stimulation. The recording site is the nucleus of the third nerve. The bar indicates illumination introduced by the experimenter: (*a*) the experimenter not watching the animal; (*b*) the experimenter's gaze fixed; (*c*) the experimenter's gaze turned away from the animal. (*B*) Inward rotation of the eyeballs on stimulation of the recording site. (*C*) Five consecutive cortically induced (sensorimotor) responses in the subthalamus (negative up). (*D*) Bars indicate the first (*a*) and the fifth (*b*) presentations of clicking at five clicks per second and (*c*) sudden dimming of the light in the animal chamber. (*E*) Bars indicate the first (*a*), the third (*b*), and the seventh (*c*) presentations of clicking at 20 clicks per second.

input sometimes produced an entirely different effect on the response (Fig. 1*E*). As soon as a clicking noise was introduced, the amplitude of the response increased significantly, and it remained high throughout the clicking. However, such augmentation or restoration of the response became less and less marked as the novelty of the stimulus gradually decreased through repetition. This type of response modification thus appears to be due to the shift of attention from some previous subject of preoccupation to the novel stimulus given.

If we are to conceive of the flattening of the response by an afferent input as an inhibitory process, the sudden reappearance or restoration of the response by some afferent could be considered a manifestation of "disinhibition." Disinhibition may result from interaction between a previously operating inhibitory process and the novel stimulus. The novel stimulus evokes a shift of attention which in itself produces an inhibitory process. Since this latter inhibition is not observed, the two inhibitory processes must have cancelled each other out. External inhibition in classical Pavlovian conditioning may be a somewhat analogous process, since "unexpected" input preceding the conditioning stimulus inhibits the usual effect (*4*).

JUHN A. WADA
Department of Neurological Research, University of British Columbia, Vancouver, Canada

References and Notes

1. R. Hernández-Peón, H. Scherrer, M. Jouvet, *Science* **123**, 331 (1956).
2. J. A. Wada, *Recent Advances in Biological Psychiatry* (Grune and Stratton, New York, 1960), pp. 300–314.
3. ———, *Electroencephalog. and Clin. Neurophysiol.* **12**, 514 (1960); *ibid.*, in press.
4. I wish to thank Dr. John R. Knott, State University of Iowa, for his critical discussion of this work. This study was aided by federal mental health grant No. 609-5-129 and by the Provincial Mental Health Service of British Columbia.

29 August 1960

Volatile Factor in Culture of Insect Spermatocytes

Abstract. The in vitro differentiation of insect spermatocytes is critically dependent on the water content of the medium. The postulated "volatile factor" is accounted for in terms of a loss of water from the cultures.

When spermatocytes of diapausing pupae of the Cecropia silkworm are cultured in single hanging or sitting drops of the blood of a developing adult, they develop into spermatids and spermatozoa (*1*). It has been reported (*2*) that these striking cytological events take place only if the cultures are enclosed in a tightly sealed chamber. An examination of this phenomenon (*2*) suggested that the developing spermatocytes produce a "volatile factor" which is necessary for the growth and survival of spermatocytes. The nature of this hypothetical factor has been examined in the present investigation.

Table 1. Effect of daily ventilation of culture chambers on development of spermatocytes.

Cultures per chamber	Gas mixture (%)	Cysts counted (No.)	Developing cysts (%)
	*Cyst suspension I**		
4	Air†	804	22 (18–25)
4	O_2(20), N_2(80)‡	708	26 (12–33)
4	O_2(20), N_2(80)	901	26 (15–37)
4	O_2(10), CO_2(5), N_2(85)	606	34 (25–42)
8	Air†	1220	38 (36–46)
8	O_2(20), N_2(80)‡	1287	33 (24–40)
8	O_2(20), N_2(80)	1519	37 (35–41)
8	O_2(10), CO_2(5), N_2(85)	1659	41 (35–48)
16	Air†	1061	36 (28–55)
	Cyst suspension II		
16	Air†	260	53 (46–58)
16	O_2(2), N_2(98)	391	60 (55–62)
16	O_2(2), CO_2(5), N_2(93)	584	58 (53–63)

* Blood diluted with insect Ringer. † Not ventilated. ‡ Not saturated with water vapor.

The cultures were prepared essentially by techniques which have been described (*2*, *3*). Each culture chamber consisted of a Lucite ring sandwiched between two glass plates, the joints being sealed with melted paraffin. The internal volume of each chamber was 16 cm^3. In experiments where the chamber was ventilated, the Lucite ring was provided with inlet and outlet tubes. Up to 16 sitting-drop cultures were placed in a grid pattern in each chamber. The drops were of uniform size, but the number of cysts (*4*) in each drop varied between 50 and 300. In each case the experimental and control chambers were prepared from the same suspension of cysts. After 7 days at 25°C, four or more drop cultures were photographed. The degree of development was assessed from the photographs in terms of the percentage of cysts that had completed the meiotic divisions and had begun to elongate.

Table 1 is a summary of the results obtained in cultures ventilated daily with 125 cm^3 of the specific gas mixture given. The mixtures were saturated with water vapor before they were passed into the chamber, except in the two cases noted. The results in Table 1 show no indication of any harmful effects of the ventilation procedure.

One culture was ventilated continuously for 7 days with a gas mixture of 3 percent oxygen, 5 percent carbon dioxide, and 92 percent nitrogen equilibrated with insect Ringer's solution. The flow rate was 30 to 80 cm^3/hr. The average development in two unventilated control chambers was 25 percent, whereas the ventilated chamber showed an average development of 28 percent.

The concept of a "volatile factor" was initially derived from the observation that single drop cultures undergo little or no development if placed in a chamber in the absence of other cultures (*2*). This finding has been confirmed in the present study. Thus, a single culture enclosed in the 16 cm^3 chamber invariably degenerates. If, however, the single culture is placed in a chamber with 7 or 15 drops of blood, it may show development comparable to a drop culture enclosed in a chamber with 7 or 15 other cultures (Table 2).

In this culture technique, water always evaporates from the cultures and condenses as a visible film on the walls of the chamber. The distillation from the drop cultures is attributed to temperature gradients within the chambers, especially when the latter are examined under the compound microscope. I have also been able to show that the blood of the developing adult is ordinarily at the upper limit of concentration that can be tolerated by spermatocytes;

Table 2. Development of single drop cultures accompanied by drops of blood, compared with development of 8 or 16 cultures of the same cyst suspension.

Cultures per chamber	Cysts counted	Developing cysts (%)
8	1393	29 (25–35)
1*	217	32
8	1220	38 (34–46)
1*	201	30
16	402	43 (31–59)
1†	92	66
16	282	30 (12–53)
1†	289	18

* One drop culture plus 7 drops of blood.
† One drop culture plus 15 drops of blood.

therefore, any evaporation may render it toxic to the cysts. These observations and the experiments presented above indicate that it is unnecessary to postulate any "volatile factor" other than water vapor (*5*).

BLAIR BOWERS
Biological Laboratories, Harvard University, Cambridge, Massachusetts

References and Notes

1. E. L. Schmidt and C. M. Williams, *Biol. Bull.* **105**, 174 (1953).
2. M. M. Ketchel and C. M. Williams, *ibid.* **109**, 64 (1955).
3. H. A. Schneiderman, M. M. Ketchel, C. M. Williams, *ibid.* **105**, 188 (1953).
4. The spermatocytes of the Cecropia silkworm occur as hollow balls of several hundred cells surrounded by follicle cells. Such an aggregation of cells is called a spermatocyst. The cells within one cyst develop synchronously.
5. I am grateful to Prof. C. M. Williams for his very helpful criticism of the manuscript.

8 July 1960

Changes in Incidence of Sex Chromatin in Subcultured Cells

Abstract. Sex chromatin counts of subcultured cells of both female human mammary tumor and female rabbit kidney show a considerable drop from an initial high level. Cultures in which sex chromatin persists also retain the viral insensitivity of their source material.

The presence of sex chromatin in tissue of female origin has been demonstrated in explants and primary trypsinized cell cultures (*1–3*), but generally not in cell lines after prolonged cultivation in vitro (*1, 4*).

The first report of sex chromatin in subcultured female cells was in human mammary tumor tissue cultured for 10 weeks, through nine transfers (*1*). In another report, sex chromatin was not found in human female tissue cultures aged 2½ months to 3½ years, after nine or more transfers, but was present in "younger" cultures aged 2 to 55 days, after three to five transfers (*5*).

More recently, the presence of sex-chromatin-like chromocenters in long-term cultures of both female and male human tissues was reported (*6*). Such chromocenters were found in 5 percent of the HeLa cells studied, and in 27 percent of the D-189 cells, of male origin. Multiple chromocenters, resembling those found in D-189 and, presumably in HeLa, were also found in cell nuclei in a study of 15 successive passages of stock HeLa cells maintained in our laboratory, but we found no typical sex chromatin, as described by Barr *et al.* (*7*).

Since the reported "sex-chromatin-like chromocenters" were found in male as well as in female subcultures, in contrast to other negative findings of sex chromatin in cultures of male origin (*5*), these counts may have included chromatin clumps simulating sex chromatin. The alteration of the distribution of sex chromatin normally found in explants and primary cultures that occurs with prolonged subculturing could be due either to actual loss of sex chromatin or to its masking by increased clumping of the chromatin granules. In either case, these nuclear changes could provide a useful marker of in vitro cell transformation.

The human mammary tumor cell line in which the presence of sex chromatin was first reported (*1*) subsequently was maintained through 24 weeks and 18 transfers, in Lactal (*8*) with human, horse, or rabbit serum. During the subculturing, sex chromatin dropped steadily, from a high of 63 percent to a final count of 9 percent. After the 19th transfer, this culture failed. Therefore it seemed desirable to follow sex chromatin changes in an uninterrupted culture.

Accordingly, counts have been made of the sex chromatin in a line of rabbit kidney cells from their initial cultivation to the present. These cells started as a trypsinized suspension of kidney from a female New Zealand rabbit. The medium was a modified Lactal with cow serum (*9, 10*). At the time of the last count, this culture had surpassed the human mammary tumor line in both duration of maintenance (38th week) and number of transfers (20th). Its continuing vigor is indicated by the fact that at the third day after transfer the number of cells was doubling in 24 hours and an average of 10 percent of the cells were undergoing mitosis.

The following characteristics found in primary explants were used as criteria for sex chromatin in the nuclei of the subcultured cells: (i) one to three well-defined nucleoli in nucleoplasm composed of relatively fine granules which are Feulgen-positive and deeply basophilic with hemotoxylin-eosin staining, and (ii) a wedge-shaped or plano-convex sex chromatin mass, larger than any of the Feulgen-positive granules and more basophilic than the nucleoli. Nuclei with large multiple chromatin clumps were not counted.

Sex chromatin both adjacent to and free of the nuclear membrane was counted in 200 cells from duplicate cultures from each passage, with the exception of the last count (38th week) of the rabbit kidney cells. Because the incidence of sex chromatin was declining, the procedure for that count was modified to reduce the possibility of counting chromatin clumps of any size. Duplicate cultures of two successive days of cultivation were fixed and stained with hemotoxylin and eosin, and in each slide 25 random fields were examined at a magnification of 1000. Only the most typical sex chromatin masses were counted in nuclei with the specified characteristics, and even deeply stained chromatin masses were rejected if they were small, spherical, or not adjacent to the nuclear membrane. Sex chromatin was found in all four of the cultures, and the average did not vary significantly from earlier counts (Fig. 1).

As Fig. 2 shows, there was no significant change, between the primary

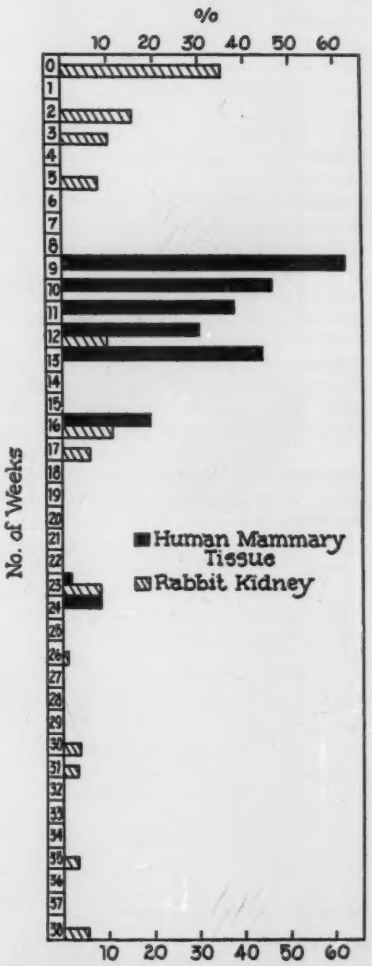


Fig. 1. Percentage of sex chromatin in maintained cultures of female human mammary tumor and of female rabbit kidney cells, by number of weeks. Percentages are average counts of duplicate cultures fixed and stained 3 to 5 days after transfer. Human mammary tumor cultures were not available for counting until the 9th week, representing the 5th transfer. They terminated during the 25th week, after the 19th transfer. Rabbit kidney cultures at the 38th week represent the 20th transfer.

and the last culture, in cell morphology or in the size of nuclei or sex chromatin.

In early transfers of both the human mammary tumor and the rabbit kidney cell lines, counts correspond, respectively, to the incidence of sex chromatin in somatic human tissue (*7, 11*) and in explants and primary cultures of cells of rat (*3*), dog, and cat (*12*). Although sex chromatin incidence in early transfers was higher in the human tumor than in the rabbit cells, in both cell lines it dropped with subculturing to 2 to 9 percent (Fig. 1).

Both cell lines also retained the insensitivity of their source material to certain viruses. In contrast to such established human cell lines as HeLa and H.Ep.No.1 (*13*), the human tumor cultures did not support the virus of infectious bovine rhinotracheitis. In contrast to an established rabbit-kidney cell line obtained from Drew (*14*) and propagated further in this laboratory, preliminary studies with our rabbit kidney cultures indicate that, up to the current passage, they fail to support poliovirus.

Culturing of the rabbit kidney cells continues for the purpose of investigating any relationship between a possible complete loss of sex chromatin and concomitant changes in morphology and viral sensitivity (*15*).

ERNEST V. ORSI
ROSLYN E. WALLACE
HILDA B. RITTER

Lederle Laboratories,
American Cyanamid Company,
Pearl River, New York

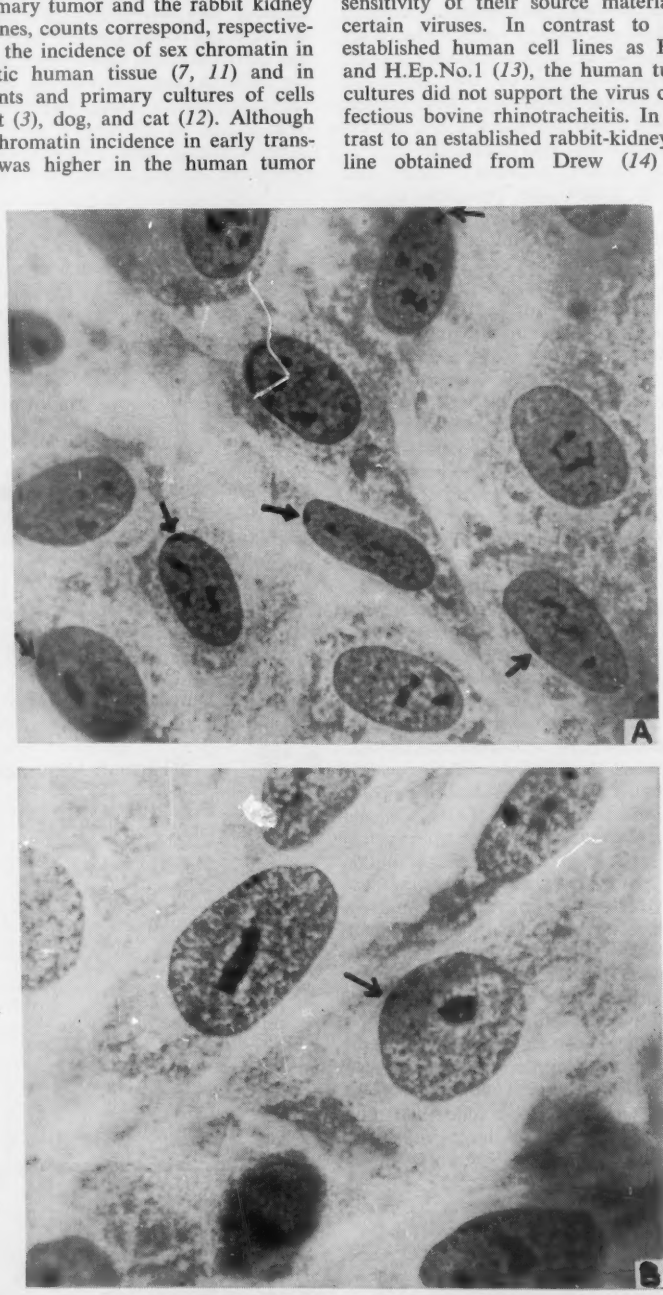


Fig. 2. Female rabbit kidney cultures, about × 1300, Wratten green filter No. 11, hemotoxylin and eosin stained. Arrow indicates sex chromatin. *A*. Primary culture, sex chromatin 35 percent. Width of nuclei average is 14 μ, range 8 to 24 μ. Average size of sex chromatin: width 1.2 μ, length 1.6 μ. *B*. 38th week, 20th transfer, sex chromatin 6 percent. Width of nuclei average is 14 μ, range 8 to 28 μ. Average size of sex chromatin: width 1.1 μ, length 1.8 μ. Culture retains whorl-like arrangement of cells and oval nuclei and elongated cytoplasm of earlier transfers. Note typical wedge-shaped chromatin mass larger than nearby fine chromatin granules.

References and Notes

1. E. V. Orsi and H. B. Ritter, *Exptl. Cell Research* **15**, 244 (1958).
2. D. M. Serr, M. A. Ferguson-Smith, B. Lennox, J. Paul, *Nature* **182**, 124 (1958).
3. C. P. Miles and A. S. Koons, *Science* **131**, 740 (1960).
4. C. P. Miles, *Cancer* **12**, 299 (1959).
5. ———, *Nature* **184**, 477 (1959).
6. S. H. Dewitt, A. S. Rabson, F. Y. Legallais, P. R. Del Vecchio, R. A. Malmgren, *J. Natl. Cancer Inst.* **23**, 1089 (1959).
7. M. L. Barr, L. F. Bertram, J. A. Lindsay, *Anat. Record* **107**, 283 (1950).
8. J. L. Melnick, J. T. Riordan, *Proc. Soc. Exptl. Biol. Med.* **81**, 208 (1952).
9. R. Wallace, M. C. Davies, B. Pease, M. Englert, A. W. Moyer, *Proc. Soc. Exptl. Biol. Med.* **103**, 845 (1960).
10. A paper by R. E. Wallace, E. V. Orsi, H. B. Ritter, and A. W. Moyer, describing details of the culturing method, is in preparation.
11. R. H. Prince, M. A. Graham, M. L. Barr, *Anat. Record* **122**, 153 (1955).
12. H. Burlington, *Exptl. Cell Research* **16**, 218 (1959).
13. M. Stebbins and B. Klaver, personal communication.
14. R. Drew, *Science* **126**, 747 (1957).
15. We are grateful to Leslie McWilliams for the photomicrographs, to John Turpanjian for growing the mammary tumor cells, to Esther Chasan for help in preparation of the manuscript, and to Barbara Balogh for technical assistance.

7 September 1960

Excessive Stimulation of Salivary Gland Growth by Isoproterenol

Abstract. In the rat, chronic treatment with isoproterenol can cause a selective growth of the salivary glands to approximately five times their normal size within 17 days. This enlargement is principally due to mitotic proliferation and hypertrophy of the parenchymatous cells.

It was recently observed that chronic treatment with very large doses of isoproterenol is tolerated by the rat if the compound is administered intraperitoneally. By this procedure, certain otherwise undetectable actions of this catecholamine became evident (for example, production of aortic aneurisms and nephrocalcinosis). In the course of this work it was incidentally

noted that rats chronically treated with isoproterenol secrete an extraordinarily large amount of very viscous saliva, with the result that the fur over most of the body surface is constantly moist (*1*).

The data reported here show that this excessive salivation is due to a true sialadenotrophic action of isoproterenol; the compound is not merely a sialagogue but a potent and selective stimulator of salivary gland growth.

Thirty female rats of the Holtzman strain, with a mean initial body weight of 134 g (range, 130 to 140 g), were subdivided into two equal groups. Group 1 was treated with 50 mg of isoproterenol in 0.2 ml of water, twice daily, intraperitoneally, while group 2 acted as untreated controls. Six animals of group 1 died during the course of the experiment, showing obvious enlargement of the salivary glands; the rest were killed, together with the controls, after 17 days of treatment. The salivary glands of all the sacrificed animals were fixed (in SUSA solution saturated with picric acid) for subsequent weighing and histologic [Periodic Acid Schiff (PAS), hematoxylin-phloxine] study. In the treated rats, the enlargement of the salivary glands (Fig. 1) was so pronounced that it could easily be recognized during life by mere inspection and palpation of the neck region. The weight range of the control glands was 333 to 516 mg, as compared with 2531 to 2574 mg after treatment.

Histologic study revealed that the enlargement of the salivary glands is almost entirely due to intense mitotic proliferation of the serous, mucous, and duct cells; it is accompanied by microscopic evidence of increased secretory activity. The stroma showed only a moderate degree of edema, and imbibition with slightly PAS-positive material. The parotid, submaxillary, and sublingual glands were enlarged to approximately the same degree, whereas the external lacrimal gland remained essentially unaffected.

The true parenchymatous growth of salivary gland tissue thus induced experimentally bears little resemblance to the various types of clinical sialadenitis (for example, postoperative parotitis, uveoparotitis), the latter being essentially inflammatory lesions. However, the changes produced by isoproterenol are structurally similar to the "idiopathic," true hypertrophies and hyperplasias of the human salivary glands that have been described as "sialadenoses" in patients suffering from various endocrine and nervous diseases (see *2*). A similar selective parenchymatous growth of the salivary glands has also often been reported to occur in man as a result of malnutrition and psychic stress. During World War II this condition apparently assumed epidemic proportions among the inmates of the ghetto of Warsaw (*3*) and the concentration camp of Terezin (Theresienstadt); indeed, this type of salivary gland enlargement has even been referred to in the literature as the "symptom of Terezin" (*4*).

It remains to be seen, however, whether these clinical salivary gland enlargements are pathogenetically related to that produced experimentally by isoproterenol, and whether natural catecholamines, when elaborated in excess by chromaffin or nervous tissue, can exert similar effects under certain conditions (*5*).

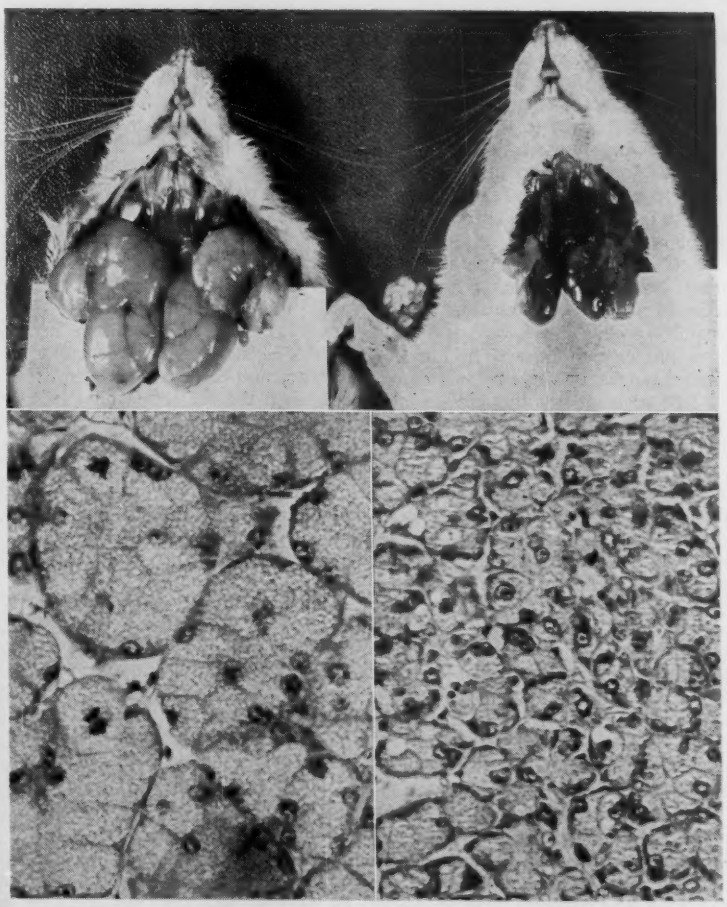


Fig. 1. (Top) Greatly enlarged salivary glands of an isoproterenol-treated rat (left) in comparison with salivary glands of an untreated control. (Bottom, left) Mitotic proliferation and cellular hypertrophy in the parotid gland of an isoproterenol-treated rat, in comparison with (right) cells in an untreated control (× 420).

HANS SELYE
RENE VEILLEUX*
MARC CANTIN†
Institut de Médecine et de Chirurgie expérimentales, Université de Montréal, Montreal, Canada

References and Notes

1. H. Selye, E. Bajusz, R. Veilleux, *Cor et Vasa*, in press.
2. W. Kley, *Münch. med. Wochschr.* **101**, 997 (1959); S. Rauch, *Schweiz. med. Wochschr.* **86**, 771 (1956).
3. F. Braude-Heller, *Am. JOINT Distribution Comm.* (Warsaw, 1946).
4. J. Flusser, V. Chvojková, J. Zabka, *Sbornik, pathofysiol. trávení vyživy* **5**, 11 (1951).
5. This study was supported by grant No. B-2037 (C1) from the National Institute of Neurological Diseases and Blindness and by grant No. A-1641 (C2) from the National Institute of Arthritis and Metabolic Diseases, U.S. Public Health Service. The isoproterenol was obtained from Winthrop Laboratories.

* Fellow of the National Research Council of Canada.
† Fellow of the Quebec Heart Foundation, Inc.

22 August 1960

Meetings

Organization of Scientific Research in Latin America

A regional meeting to discuss the organization of scientific research in Latin America was held from 3 to 7 October 1960 in the Central University of Venezuela, Caracas. The meeting was arranged by the UNESCO Science Cooperation Office for Latin America, under the patronage of the Ministry of Education and the University of Venezuela. Heads of national research councils, rectors of universities, deans of science faculties, and senior scientists from Argentina, Bolivia, Brazil, Chile, Colombia, Cuba, Ecuador, Mexico, Peru, Uruguay, and Venezuela had been invited to attend, and the World Health Organization and the National Academy of Sciences (U.S.) sent observers. The meeting was held in the beautiful buildings of the Central University.

The President of the Republic, Rómulo Betancourt, spoke briefly at the opening ceremony, welcoming the delegates with the assurance that they would find in the Venezuela of today complete freedom for the development of scientific research. Other speeches were delivered by A. Establier, head of the UNESCO Science Cooperation Office for Latin America, Rafael Pizani, minister for education, and Francisco De Venanzi, rector of the Central University.

The meeting elected De Venanzi as its chairman. The working sessions were opened by a review of the general tendencies of scientific research in Latin America by Bernardo Houssay, president of the Council for Scientific and Technical Research of Argentina. This paper provoked a valuable discussion which formed a background for the other papers presented at the meeting.

The paper by David Stitchkin, rector of the University of Concepción, Chile, on funds available for scientific research, with special reference to equipment, was the one which caused least discussion, since the meeting was unanimous in concluding that the amounts presently available are notably insufficient. It was recommended that governments should accept as a target the allocation of 2 percent of the national budget for scientific research.

During the discussion of the paper by Mario Gonzalez (Cuba) on the basic and applied sciences, it became clear that the meeting did not wish to emphasize the distinction between the two and preferred to think of science as a whole, recommending that firms in industry and agriculture should strengthen their links with research and teaching institutions in view of the profound effect which science has on modern commercial life.

Houssay introduced the question of national research councils, which exist in only a very few Latin American countries. The meeting recommended that other governments of the region give serious thought to the advantages of establishing research councils, and UNESCO was asked to provide information to governments about the functions and possible types of organization of research councils.

Marcel Roche, director of the Venezuelan Institute of Scientific Research, presented a paper on the career of the research worker. He analyzed and compared the careers offered by the research councils of Argentina, France, and Venezuela. It was thought that the arrangements adopted by the Argentine and Venezuelan councils, whereby members of their staffs are able simultaneously to accept teaching posts, are valuable in the Latin American setup, since this makes maximum use of the small scientific manpower available and keeps the research worker in touch with universities and youth. This subject was very closely related to the next one discussed, the shortage of teaching and research personnel in Latin America, which was introduced by Rodolfo Talice, dean of the Faculty of Science at the University of Montevideo.

One of the highlights of the meeting was the paper by Paulo Sawaya, dean of the faculty of philosophy of the University of São Paulo, on the results of adopting in certain universities and institutions the full-time system. Most universities and research organizations permit their staffs to hold one or more posts outside the organization, and the virtues and vices of this system form one of the most hotly debated subjects in scientific circles in Latin America. The meeting recommended that governments and universities establish the full-time system as the ideal in research and higher teaching posts, and that they provide salaries and working conditions adequate for this purpose.

UNESCO has encouraged and assisted in the formation of regional research centers, such as that for mathematics in Buenos Aires, and of groupings of research centers, such as the Latin American Council for Cosmic Radiation. Ismael Escobar, head of the Cosmic Ray Physics Laboratory at Chacaltaya, Bolivia, introduced this topic. Discussion led the meeting to call on UNESCO to continue its efforts in this field, so that teams of research workers may be brought together, animated by the desire to achieve Latin American unity in research.

De Venanzi analyzed the attitudes of governments and of public opinion toward scientific research problems in Latin America. Though much improvement has occurred in the last few years, a great deal remains to be done. The meeting felt that the press, radio, and television have a paramount role to play and hoped that ways can be found to establish training in scientific journalism. In this connection, delegates were happy to note the complete and accurate coverage of the meeting in the Caracas press.

In Latin America, fellowships tenable in more scientifically developed areas will, for some time to come, provide the principal source of higher training for research workers in many fields. E. Beltran, under-secretary for forestry and game resources in Mexico, discussed the subject in all its aspects. An increase in the number of fellowships granted by governments and other agencies was recommended, as well as greater emphasis on instruction in foreign languages, since language deficiencies frequently make it impossible to derive full benefit from fellowships. The paper by M. A. Garrido Malo, dean of the science faculty at San Marcos University, Lima, was on a closely allied subject: exchange of scientists between Latin American countries. UNESCO was asked to publish its *Boletin* with greater frequency, so that news of courses, special facilities, visits of foreign scientists, and so on may be more rapidly disseminated, and all laboratories were urged to use to the utmost the possibilities offered.

The subject of scientific documentation in Latin America was introduced by Manuel Sadosky, vice-dean of the science faculty of the University of Buenos Aires. A lengthy discussion led to a series of recommendations: that UNESCO should make a survey of scientific journals in Latin America, with the object of formulating a plan for ra-

Kodak reports on:

strange dances in the movies . . . what Gutenberg might have done with photography . . . the deftness of enzymes

Favor for the high-speed congress

Dust Performs for Plant's Pollution-Control Movies, *Chem. Week*, 84:84, 86, May 2, 1959. (Procter &Gamble uses high-speed motion-picture sequences for the qualitative control of in-plant dust.)

The Ignition of Explosives by Radiation, J. Eggert, *J. Phys. Chem.*, 63:11-15, Jan., 1959. (High-speed photography proves that the detonation of nitrogen iodide starts before the light flash ends, showing that only a fraction of the energy is used for the detonation.)

Time after time we have visited a customer proud of some accomplishment with high-speed movies. He is willing to show us—eager, delighted to show us. The projector is started and we watch. We see a collection of strange objects. We don't know for sure what they are. Little seems to be happening. After quite a while, a new object enters the scene from the left. Shortly another new object comes up from the bottom. The two dance around each other, touch, and exit from the top of the frame. All is again static on the screen. After another while the reel comes to its end and we jump to our feet exclaiming hearty congratulations.

He deserves congratulations, probably. If we had lived with the problem as he has, the objects in the picture might have seemed no stranger than the face in the bathroom mirror; the dance might have been the triumphant, forceful, sudden, undisputed clincher to a vexatious problem; the all-purpose enthusiasm of the born salesman might have meant more.

Nevertheless, we need not be ashamed. We help scientists and engineers use high-speed photography by manufacturing a group of films to the stringent mechanical requirements of high-speed cameras. *Kodak Plus-X Reversal Film* we make for reversal processing to a fine-grain positive. *Kodak Tri-X Reversal Film* is four times as fast. *Kodak Double-X Panchromatic Negative Film*, which is a bit faster yet and very sharp, is picked when a quick negative will suffice or when several prints may be wanted later. *Kodak Royal-X Pan Recording Film* is picked only when light is very limited indeed; *Kodak Linagraph Ortho Film*, for accentuated sensitivity to green light; *Kodak High Speed Infrared Film*, for sensitivity to 9000A, with a maximum from 7700A to 8400A; *Kodachrome Film*, for color, with low-cost commercial processing widely available; *Ektachrome ER Film*, for color at exposure index of 160 or higher.

Another thing. A bibliography on high-speed photography. Every item our library knows. Forty-six pages of items like the specimens at the immediate left. No pictures, though. No charge either. Coverage extends into 1960. Got it ready to distribute to the Fifth International Congress on High-Speed Photography in Washington in October.

Eastman Kodak Company, Photorecording Methods Division, Rochester 4, N. Y., would be glad to send the bibliography or answer questions about the above-named films.

Try these paragraphs:

Routine commercial news item: *Kodak Phototypesetting Film* and *Kodak Phototypesetting Paper* are now sold by your* Kodak dealer.

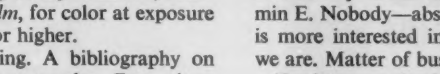
Deeper historical significance: Gutenberg did a fine thing by inventing movable type. The fellows who improved on his idea with hot-lead-casting typesetting machines also did their bit for civilization. Now, however, too many authors want to convey too many complicated thoughts to too many splinter groups of readers. The hot-lead machines are at their best with neat paragraphs of well-carpentered prose. Well-carpentered prose has its place, but for expressing the more severely logical varieties of thought it is limiting, imprecise, unclear, windy, and cumbersome. A more agile symbolism is needed at popular prices. Alert printing houses are trying to provide this symbolism through photographic methods rather than through the brutish hewing of lead. Give them time and encouragement. We have added our little touch of encouragement by having these two paragraphs phototypeset. Whether severely logical or not, they look all right, don't they?

Creatine dissembled

Eastman 7911 N-Amidinoalanine 10 g. ..$4.80

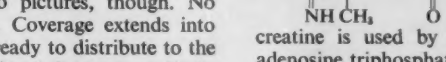
Also known as dl-α-guanidinopropionic acid. Physiologists call it alacreatine. Physiologists want to know it better. Some physiologists, anyway. Particularly those interested in vitamin E. Nobody—absolutely nobody—is more interested in vitamin E than we are. Matter of business.

Deplete an animal of vitamin E and creatine shows up in urine. Creatine is



Normally creatine is used by combining with adenosine triphosphate to make phosphocreatine. After phosphocreatine yields up its energy, creatinine is left. Creatinine is anhydride of creatine. Vitamin E somehow mixed up in this. Creatine-to-creatinine ratio in urine is therefore good index of vitamin E status. OK.

Alacreatine is



Note that difference from creatine is position of methyl group. Feed alacreatine to rats and what happens in 6 weeks? They become very weak, as in nutritional muscular dystrophy from lack of vitamin E (*Nature*, *187*, 421). (Different etiology from human muscular dystrophy.)

Does alacreatine take place of genuine creatine in combining with ATP? Good question. Good answer could come from someone who buys our alacreatine for further studies. Might beat us in learning new fact about behavior of vitamin E. Would be consolation to know he at least used our alacreatine.

We make alacreatine by reacting thiourea with ethyl bromide to yield ethyl isothiourea hydrobromide, then add this with alkali to alanine. Product splits out with ethyl mercaptan. Ethyl mercaptan stench pretty well worn out as subject for levity.

Nature makes creatine by two-step method also. In kidney an amidine group from arginine transfers to glycine to make glycocyamine. In liver the glycocyamine takes on methyl group from methionine, becomes creatine. It's all done with enzymes. Nature neater, cheaper, makes more useful product.

If inconvenient to get from nature, get Creatine *from us also as Eastman 951. Also offer* Creatinine *as Eastman 918.* Creatinine Hydrochloride *as Eastman 7642,* Creatinine Zinc Chloride *as Eastman 1272, and some 3800 other Eastman Organic Chemicals. Complete catalog from Distillation Products Industries, Rochester 3, N. Y. (Division of Eastman Kodak Company).*

Price subject to change without notice.

Kodak

Everybody, more or less, has a Kodak dealer. One person can have several different Kodak dealers, even as one person at different times can have different interests and needs. If you ever hear of a Kodak product that interests you, never fester in doubt as to where to turn. Just write "Eastman Kodak Company, Rochester 4, N. Y." on the front of a postcard and write your question, name, and address on the back. Don't forget to mail it.

This is another advertisement where Eastman Kodak Company probes at random for mutual interests and occasionally a little revenue from those whose work has something to do with science

tionalizing them; that the Mexican Scientific Documentation Center should make its services more easily available to scientists in other countries; that more national scientific documentation centers should be established; that governments should grant free postal services to scientific journals; and that financial help be given to a select number of journals.

The final subject on the agenda was a review of UNESCO's science programs, particularly that of the Latin American Science Cooperation Office in Montevideo. Establier described proposals which will be debated at the general conference of the organization to be held in Paris in November, and also outlined a series of long-term projects which might be undertaken by the Montevideo office. Among these was one for an International Andean Year, during which teams of specialists in different fields would attack the problems of this vast mountain chain which so profoundly affects living conditions in the countries through whose territories it runs. Another proposal was for a full-scale operation directed toward rationalizing scientific journals. A third would deal with the problems of the unproductive areas of the seas, lakes, and rivers of the continent. At the end of this discussion, Establier received the warm congratulations of the meeting, both for the way he has directed UNESCO's science activities in Latin America and for the organization of the Caracas meeting.

The final act of the meeting was the approval of a statement which it was hoped would come to be known as the "Caracas Charter," in which the delegates summed up their views on science organization in Latin America. The text is as follows.

The delegates attending the Seminar on the Organization of Scientific Research in Latin America, held in the City of Caracas from 3 to 7 October 1960, on the initiative of UNESCO and the Central University of Venezuela:

Considering:

That although considerable progress has been achieved in the field of scientific organization in some countries of Latin America, nevertheless they are not on the same level as the most advanced countries, nor is there a sufficient number of research teams to cover the needs of Latin America;

That the experience of highly developed countries demonstrates that the most remunerative investment that can be made is in scientific and technical research;

That in order to overcome the situation of insufficient economic and cultural development, the encouragement of research, especially in the basic sciences, is indispensable;

That knowledge of science and its applications should be introduced and developed at all levels of education, and that it is at the secondary level that scientific vocations and talents can be detected;

That public opinion should be aware of the role and importance of science and of the achievements of Latin American research workers;

Declare:

That a reevaluation of the organization of scientific research is indispensable, according to it due priority among the problems and prospects of Latin America:

That in order to carry out effective scientific activities not less than 2 percent of the national budget is required;

That special attention should be given to the achievement of high-level efficiency in the teaching of the basic sciences;

That encouragement should be given to research workers by means of the full-time system, with a salary able to provide a decent standard of living;

That many young students and graduates with gifts for research should be able to obtain fellowships, tenable within or outside of their countries, and working conditions which will allow them to develop their capabilities;

That the establishment of national scientific and technical research councils should be encouraged, in view of the success which these have had in the more developed countries and in several Latin American states;

That, similarly, assistance by the more advanced universities of Latin America to those less well developed should be encouraged;

That newspapers, and radio and television stations should give special attention to the diffusion of scientific knowledge and of information about scientific work in each country, for which purpose the training of specialized journalists, capable of informing the masses as part of their important mission, about the discoveries and the benefits obtained from high-level scientific and cultural activity should be encouraged;

That governments, members of parliament, business men and in general all citizens should, in one way or another, seek the opinion of scientists and technologists of good standing before they take fundamental decisions affecting the destinies of the countries of Latin America.

The hospitality shown by the Government and Central University of Venezuela was on a princely scale. The President of the Republic took a close personal interest in the meeting and accorded the members an audience in Miraflores Palace. We were given an opportunity to see the different departments of the university and the laboratories of the Venezuelan Institute of Scientific Research, magnificently installed at La Pipe near Caracas. We left Caracas firmly convinced that scientific research in Venezuela is at the dawn of a glorious future.

BERNARDO HOUSSAY
Council of Scientific and Technical Research of Argentina, Buenos Aires

Forthcoming Events

January

25–27. Mathematical Assoc. of America, annual, Washington, D.C. (H. L. Alder, Dept. of Mathematics, Univ. of California, Davis)

26–27. Western Spectroscopy Conf., 8th annual, Pacific Grove, Calif. (R. C. Hawes, Applied Physics Corp., 2724 S. Peck Rd., Monrovia, Calif.)

27–28. Royal College of Physicians and Surgeons, annual, Ottawa, Ontario, Canada. (T. J. Giles, 150 Metcalfe St., Ottawa)

28–30. Control of the Mind, symp., San Francisco, Calif. (Dept. of Continuing Education in Medicine, Univ. of California Medical Center, San Francisco 22)

28–31. Infertility, sectional meeting, Intern. Fertility Assoc., Acapulco, Mexico. (M. L. Brodny, 4646 Marine Dr., Chicago 40, Ill.)

29–3. American Inst. of Electrical Engineers, winter meeting, New York, N.Y. (E. C. Day, AIEE, Technical Operations Dept., 33 W. 39 St., New York 18)

30–3. Clinical Cong. of Abdominal Surgeons, Miami Beach, Fla. (B. F. Alfano, 663 Main St., Melrose 76, Mass.)

30–4. American Library Assoc., midwinter meeting. (Mrs. F. L. Spain, New York Public Library, 20 W. 53 St., New York, N.Y.)

31–4. American Assoc. of Physic Teachers, New York, N.Y. (F. Verbrugge, 135 Main Engineering, Univ. of Minnesota, Minneapolis)

31–4. American Physical Soc., annual, New York, N.Y. (K. Darrow, APS, Columbia Univ., 116th St. and Broadway, New York)

February

1–3. Solid Propellant Rocket Conf., American Rocket Soc., Salt Lake City, Utah. (R. D. Geckler, Aerojet-General Corp., P.O. Box 1947, Sacramento, Calif.)

1–3. Winter Military Electronics Conv., 2nd, Inst. of Radio Engineers, Los Angeles, Calif. (A. N. Curtiss, IRE Business Office, 1435 S. La Cienega Blvd., Los Angeles 35)

1–4. American Physical Soc., annual, New York, N.Y. (K. K. Darrow, APS, 538 W. 120 St., New York 27)

2–4. Congress on Administration, 4th annual, Chicago, Ill. (R. E. Brown, American College of Hospital Administrators, 840 N. Lake Shore Dr., Chicago 11)

6–8. American Acad. of Allergy, 17th annual, Washington, D.C. (J. O. Kelly, 756 N. Milwaukee St., Milwaukee 2, Wis.)

6–8. Geodesy in the Space Age, symp., Ohio State Univ., Columbus. (W. A. Heiskanen, Ohio State Univ., 1314 Kinnear Road, Columbus 12)

6–10. British Medical Assoc., annual, Auckland, New Zealand (E. Grey-Turner, B.M.A., Tavistock Sq., London, W.C.1)

9–15. Second Allergy Conf., Nassau, Bahamas. (I. M. Wechsler, P.O. Box 1454, Nassau)

13–16. American Soc. of Heating, Refrigerating and Air-Conditioning Engineers, Chicago, Ill. (R. C. Cross, 234 Fifth Ave., New York 1)

14–15. Conference on Microdosimetry, 2nd, Rochester, N.Y. (N. Kreidl, Bausch & Lomb Optical Co., Inc., Rochester 2)

15–17. International Solid-State Circuits Conf., Philadelphia, Pa. (J. J. Suran, Bldg. 3, Room 115, General Electric Co., Electronics Park, Syracuse, N.Y.)

16–18. Biophysical Soc., annual, St. Louis, Mo. (W. Sleator, Dept. of Physiology, Washington Univ., St. Louis 10)

22–25. American Educational Research Assoc., annual, Chicago, Ill. (G. T. Buswell, 1201 16th St., NW, Washington 6)

23–25. American Orthopsychiatric Assoc., annual, New York, N.Y. (Miss M. F. Langer, 1790 Broadway, New York 19)

23–25. Fifteenth Annual Symp. on Fundamental Cancer Research, Houston, Tex. (Publications Dept., Univ. of Texas M.D. Anderson Hospital and Tumor Inst., Texas Medical Center, Houston 25)

23–25. Symposium on Molecular Basis of Neoplasia, Houston, Tex. (Publications Dept., Texas Medical Center, Houston 25)

26–1. American Inst. of Chemical Engineers, natl., New Orleans, La. (F. J. Van Antwerpen, AICHE, 25 W. 45 St., New York 36)

26–2. American Inst. of Mining, Metallurgical, and Petroleum Engineers, annual, St. Louis, Mo. (AIME, 29 W. 39 St., New York 18)

27–3. Conference on Analytical Chemistry and Applied Spectroscopy, 12th, Pittsburgh, Pa. (L. P. Melnich, U.S. Steel Corp., Monroeville, Pa.)

(See 16 December issue for comprehensive list)

New Products

The information reported here is obtained from manufacturers and from other sources considered to be reliable. Neither Science *nor the writer assumes responsibility for the accuracy of the information. All inquiries concerning items listed should be addressed to the manufacturer. Include the department number in your inquiry.*

■ AUTOMATIC SAMPLE CHANGER holds as many as 49 test tubes containing gamma-emitting samples. During operation the test tubes are automatically lowered in proper sequence into the well crystal of a shielded scintillation detector. A printing timer records sample identity and time for preset count. (Nuclear-Chicago Corp., Dept. Sci728, 359 Howard Ave., Des Plaines, Ill.)

■ AIR SAMPLER automatically collects dust samples on paper tape that is advanced periodically to provide a record of air pollution. Provisions are incorporated for accessory internal evaluating attachments including a paper densitometer, an optical evaluator, and a scintillation or Geiger counter. Sensitized tapes can be prepared for detection of toxic gases. Sampling intervals may be chosen from 1 per min. to 1 every 2 hrs. Air is drawn through ½-in. sample spots at approximately 14 lit./min. (Gelman Instrument Co., Dept. Sci977, P.O. Box 66, Chelsea, Mich.)

■ CIRCUIT BOARD DRILLING MACHINE, controlled by magnetic tape, is capable of drilling 40 holes per minute with each drill head. Hole positioning accuracy is said to be ±0.001 in. Programing is accomplished by inserting either an etched master board or the negative to be used for contact printing and performing the drilling sequence manually, using an optical comparator with magnification of 20 to position the drill. Playback is accomplished at 4 times the programing rate. (Micro-Path, Inc., Subsidiary of United Industrial Corp., Dept. Sci978, Los Angeles, Calif.)

■ PLASTIC TUBES of polyvinyl are designed to be readily connected to other tubing or apparatus by means of an integral tapered connector end or integral funnel end. Tubing is said to be odor-free, taste-free, and nontoxic. All except oxygen tubes are clear white. Oxygen tubes are transparent medium green. (A. S. Aloe, Dept. Sci972, 1831 Olive St., St. Louis 3, Mo.)

■ RESISTANCE THERMOMETER ELEMENTS are mounted on a stainless-steel shim overmolded with silicone rubber; they are designed to be strapped on or around surfaces. A wide range of shapes and sizes is offered. (Arthur C. Ruge Associates, Dept. Sci986, Hudson, N.H.)

■ LABORATORY POWER PANEL for use in teaching is available for rack or cabinet mounting. It provides continuously variable high- and low-voltage a-c and d-c; d-c transistor and bias supply; a-c filament and rectifier source; continuity testing source; line-voltage outlets; and metering. Each unit provides complete service for two students. Input is 115 volts a-c. (Buck Engineering Co., Dept. Sci983, 37–41 Marcy St., Freehold. N.J.)

■ PORTABLE OSCILLOSCOPES, fully transistorized, will operate on internal rechargeable batteries, a-c line power, or low-voltage d-c. Models are available with 1-, 2-, or 3-in. display. Size of the 1-in. model is 2¾ by 3¼ by 5½ in. Frequency range is d-c to 1.5 Mcy/sec. Sweep range extends in five calibrated steps to 1 μsec per division and sensitivity in seven steps to 0.1 volt per division. Input impedance is 1 megohm. Triggering is provided from a plus or minus slope with variable amplitude control. (Electro Instruments Inc., Dept. Sci979, 1165 Morena Blvd., San Diego 10, Calif.)

■ LIGHT MODULATOR is an electro-optical device said to be capable of providing large-aperture exposures at speeds as great as 100 μsec and with an indefinite exposure limit. The device utilizes a glass plate mounted between a pair of rigid beams. Placed at either end of the beams are stacks of piezoelectric drivers. Excitation of the drivers transmits strain to the glass plate which becomes double refracting and changes the state of polarization of transmitted light. Excitation voltage requirement is about 3000. (Electro-Optical Systems, Inc., Dept. Sci980, 125 N. Vinedo Ave., Pasadena, Calif.)

■ TRAINING MICROSCOPE that permits instructor and student to examine a specimen simultaneously includes two Stereo-Zoom microscopes and two accessories; a 0.5 times lens attachment to increase working distance, and a vertical illuminator that acts as a beam splitter and permits both viewers to see the same field with equal clarity. Each microscope can also be used independently. (Bausch and Lomb Optical Co., Dept. Sci984, Rochester 2, N.Y.)

■ INTEGRATOR operates directly from a millivolt signal and is capable of integrating without use of a recorder. The output consists of pulses at rates up to 10,000 per minute. Models for rates of 1000 per minute or less have an indicating counter and contact-closure output. Current-input models permitting operation in series with direct-writing recorders with 1 ma span are available. (Royson Engineering Co., Dept. Sci987, Hatboro, Pa.)

■ SOUND-LEVEL METER manufactured by Dawe Instruments Ltd., London, is fully transistorized and battery operated. The meter uses a piezoelectric-crystal, diaphragm-type microphone that feeds into a impedance-matching circuit followed by a high-gain amplifier, an 11-position attenuator calibrated in 10-db steps, and standard weighting networks. Weight is 4 lb and size is 8¼ by 5¾ by 3¾ in. Three dry cells furnish power for 60 hours' operation. (Korfund Co., Dept. Sci981, 48-250 32nd Place, Long Island City, N.Y.)

■ FOUR-CHANNEL ANALYZER, model 716, is designed for counting pulses of random spacing and amplitude. Pulses terminating between the settings of the upper- and lower-limit discriminators of each channel are passed to the output of that channel. Channel widths can be adjusted between 0 and 10 or 0 and 20 volts from the front panel; they are said to hold constant within ±1 percent through the range 0 to 100 volts. (Interstate Electronics Corp., Dept. Sci971, Anaheim, Calif.)

■ SELF-BALANCING POTENTIOMETER uses a servoamplifier to drive the wiper to a null position. The wiper position is read on a four-digit counter as percentage of full scale. Accuracy is said to be ±0.1 percent of full scale, resolution ±0.05 percent of full scale. Response time for full traverse is 8 sec. The unit operates on 115 volt a-c. (Physical Sciences Corp., Dept. Sci988, 389 N. Fair Oaks Ave., Pasadena, Calif.)

■ FREQUENCY SIGNAL GENERATOR furnishes 5 Mcy, 1 Mcy, and 100 kcy/sec signals with stability said to be ±5 parts in 10^{10} per day after a 4-mo aging period. Frequency adjustment of 500 parts in 10^9 is provided. Operating ambient temperature range is 0° to 50°C. Output impedance is 50 ohms for the two lower frequencies and 1000 ohms for the highest frequency. The instrument is transistorized and includes an emergency battery source with an automatic switchover mechanism. (Manson Laboratories, Inc., Dept. Sci989, 375 Fairfield Ave., Stamford, Conn.)

■ TWO-CHANNEL RECORDER of servo-balancing type provides two separate and completely independent channels. Adjustable span permits full 5-in. chart width to be used for any range from 0–10 mv to 0–500 v in one model. Full-scale balancing time is said to be 1 sec, limit of error ± 1 percent of span. A variety of chart speeds is available from ½ in./hr to 16 in./min and can be changed by interchange of drive-motor assembly. Over-all dimensions are 11 3/8 by 8 5/16 by 12 3/4 in. (Varian Associates, Dept. Sci991, 611 Hansen Way, Palo Alto, Calif.)

■ EVENT RECORDER is a two-channel instrument that marks on and off times by deflection of scribers. A built-in time totalizer furnishes a counter-readout of total "on" time in hours and tenths. Standard roll-chart speeds are 1, 4, 12 and 60 in./hr. (Standard Instrument Corp., Dept. Sci985, 657 Broadway, New York 12)

■ RECORDING THERMOBALANCE automatically performs thermogravimetric studies in a vacuum or in a controlled atmosphere at temperatures to 1000°C. Temperature may be programed for a selected linear heating rate or may be maintained constant. Reaction products are removed as formed and may be collected for analysis. (American Instrument Co., Dept. Sci990, 8030 Georgia Ave., Silver Spring, Md.)

■ STUDENTS' POTENTIOMETER, model 7645, features a central reading window where the measured electromotive force appears as a row of digits and a scale interpolation; three operating ranges, 0 to 1.6, 0 to 1.16, and 0 to 0.016 volt. Limits of error are said to be ±0.0005 volt on the high range, ±0.0001 volt on the medium range, and ±0.00001 volt on the low range. (Leeds and Northrup Co., Dept. Sci995, 4934 Stenton Ave., Philadelphia 44, Pa.)

■ LOW-TORQUE BEARING consists of a bearing within a bearing, the outer ring of the inner bearing being oscillated by a built-in electromagnetic drive. This action is said to cancel out friction torque. Starting torque is the same as running torque. Under preload, torque is said to increase only slightly. According to the manufacturer, a typical bearing under 2-lb radial load and preloaded to 2-lb thrust has a starting torque of 20 dy cm as compared with 1000 dy cm for a conventional bearing under the same conditions. (Barden Corp., Dept. Sci999, Danbury, Conn.)

■ TESTING MACHINE is capable of cycling up to 20 cy/sec and of following a programed heating rate of 200°F/sec. A high-speed ram delivers up to an 8-in. stroke at 1 in./min at rated load. Full-scale ranges from 200 to 50,000 lb/in. are provided, variable without mechanical adjustment. Steady-state accuracy is said to be ±0.5 percent, dynamic accuracy ±1 percent of selected range. Temperature range is up to 3000°F. Manual and programing controls are provided for each of the loading systems. The temperature- and force-loading programs may be started simultaneously from a master switch. (Compudyne Corp., Dept. Sci1000, 695 S. Warminster Rd., Hatboro, Pa.)

JOSHUA STERN

National Bureau of Standards, Washington, D.C.

Letters

Olfactory Cues in Migrating Salmon

1) Arthur D. Hasler's recent article, "Guideposts of migrating fishes" [*Science* **132**, 785 (1960)] raises some fascinating questions. I agree with him, however, when he says he "may have overstressed the olfactory sense and its importance in migration," in discussing the cues utilized by migrating adult Pacific salmon on their trip upstream to spawning beds.

2) Reference is made in Hasler's article to a study by Wisby and Hasler in which these workers plugged the nasal sacs of migrating salmon and returned them to below a fork in the Issaquah River in Washington. When I first read the article I was struck by the fact that animals with plugged olfactory openings still "preferred" one branch over the other. The change brought about by the operation was not radical—did not reduce the choice to, say, the level of chance. It did not rule out the possibility of other controlling factors.

3) This result, I believe, is not the dramatic demonstration it should be if olfactory cues, in fact, are of primary importance in "guiding" salmon back to the "parent stream." The quotation marks in the foregoing sentence are there because the parent-stream theory is by no means as well demonstrated as Hasler leads one to believe. In addition, if one starts from this theory and accepts the implications, then one is forced to look for "cues" and stimuli which this animal can utilize in "identifying" its "own" stream and in differentiating it from other spawning streams in the Pacific Northwest. In short, the problem may be stated incorrectly.

4) H. B. Wood [*Publ. Am. Assoc. Advance. Sci. No. 8* (1939)] reports observations, for example, which led him to suspect that the temperature of the water at a fork in upstream migration governed the choice in Pacific salmon, and he points out that as the temperature differential reversed itself, salmon reversed their choice of stream. The fact that many fish are found in the parent stream could be the result of temporal relations of their life cycles which would bring them back to the area when the temperature of the parent stream favored a choice in that direction.

5) Further doubt is shed on the importance of olfactory cues in salmon migration by the lack of confirmation of conditionability of spawning adult salmon. Although the case for imprinting is not clear, the question of conditioning is difficult to support in view of the fact that Pacific salmon are generally believed to migrate (certainly by the time they have entered the fresh-water system) on empty stomachs. Furthermore, it is believed that they do not eat during migration and that the stomach itself is contracted. In the absence of evidence to the contrary it is hard to understand why salmon in this condition would respond to olfactory cues.

6) Intriguing as it is, the odor theory should be tested by direct observations on sexually mature and spawning salmon. The fact that salmon fingerlings can utilize olfactory cues does not mean that the migrating adult does, in fact, react to them.

DOUGLAS A. RAMSAY
308 West 109 Street,
New York, New York

Concerning the points raised in Ramsay's letter I have the following comments (numbered to correspond with the numbering of paragraphs in his letter).

1) Odors have a distinctiveness which permits multifold differences. Because of the infinite combinations of plant communities and soil types in a river system, no two tributaries will have identical organic content; hence the seepage will have odors of never-to-be-duplicated distinctiveness. Recently J. P. Heath [*Ecology* **41**, 381 (1960)] presented evidence that substances seeping through two stream bars induce salmon to congregate at the river mouth even though the sand bar blocks their entry.

2) The statistical analysis with the chi-square test does not support the criticism. Even though the Issaquah River carried 8 to 10 times as much water as the East Fork, the displaced and recaptured nose-plugged salmon returned at random ($p, < 0.001$).

3, 4) Salmon in the Columbia River by-pass a stream in the coastal range to swim hundreds of miles upstream to enter and spawn in their home stream, which is identical in temperature to the one nearer the mouth [see B. T. Scheer, *Quart. Rev. Biol.* **14**, 408 (1939)]. The temperature hypothesis has the same weakness as the carbon dioxide hypothesis cited in my article. The cues are not unique. While some homing salmon are known to stray, the issue here is to explain the precision of homing in the great majority.

5, 6) White salmon inherit the ability to return home, early conditioning or imprinting can alter their choice of place of return. Fingerlings transferred to a stream other than the home stream return there and not to the ancestral home stream. Some species of salmon

spend 1 to 3 years in fresh water before swimming to sea. It is the conditioning of the young and retention of this "memory" to adulthood that is important. That the adults do not feed in the later stages of stream migration is beside the point. Fish become conditioned to many scents other than food odors, notably to odors which induce alarm, schooling, and recognition of sex and to the body odor of their school mates [see A. D. Hasler, *J. Fisheries Research Board, Can.* **11**, 107 (1954)].

ARTHUR D. HASLER
Department of Zoology, University of Wisconsin, Madison

Real Professionalism

There is grave danger to an already badly mangled academic freedom in one of the recommendations you cite as emanating from a report of an agency of the influential National Education Association [*Science* **132**, 439 (1960)]. I refer to the suggestion that college faculty members be required to hold state licenses.

Implementation would be greeted with loud cheers from state legislators from the rock-ribbed coast of New York's Feinberg Law to the sun-kissed shores of California's Levering Act. The most approving chorus would be the rebel yells of southern politicians.

An instructive example in point is found in South Carolina [*A.A.U.P. Bulletin* **46**, 87 (1960)]. There the governor succeeded in forcing two *private* colleges to dismiss professors he didn't like. This was achieved by having the State Board of Education refuse to allow any students of those colleges to qualify for licenses as public school teachers.

It is well known that teachers in the public schools and publicly supported colleges of the American South are afraid to take stands in favor of local compliance with Supreme Court desegregation decisions. Any state licensing of college teachers would intensify this fear at the college level and spread it systematically into the private colleges. It is not hard to anticipate the creation of the analog for college teachers of the literacy tests for southern voters which well-educated men and women fail consistently if they are colored.

Thus, the state licensing of college teachers would be, in the present atmosphere, an additional and effective weapon in the hands of the violators of academic freedom.

LEE LORCH
University of Alberta, Edmonton

PERSONNEL PLACEMENT

CLASSIFIED: Positions Wanted, 25¢ per word, minimum charge $4. Use of Box Number counts as 10 additional words. Payment in advance is required.

COPY for ads must reach SCIENCE 2 weeks before date of issue (Friday of every week).

DISPLAY: Positions Open. Rates listed below—no charge for Box Number. Rates net. No agency commission. No cash discount. Minimum ad: 1 inch. Ads over 1 inch will be billed to the nearest quarter inch. Frequency rate will apply to only repeat of same ad. No copy changes. Payment in advance is required except where satisfactory credit has been established.

Single insertion	**$40.00 per inch**
4 times in 1 year	**38.00 per inch**

For PROOFS on display ads, copy must reach SCIENCE 4 weeks before date of issue (Friday of every week).

Replies to blind ads should be addressed as follows:
Box (give number)
Science
1515 Massachusetts Ave., NW
Washington 5, D.C.

POSITIONS WANTED

(a) **Chemistry Ph.D.**, biochemistry minor, radioisotope training, 2 years of drug development, 10 years' biological chemistry teaching experience; available for academic, research, or commercial administrative appointment. (b) **Botany** (mycology) Ph.D., 3 years biological effects of cosmic radiation research in aeromedical field, 2 years mycology research on industrial fermentations of vitamins and antibiotics; interested in commercial research or academic position. (Please write for information regarding these and other scientists in all fields; nationwide service.) S1-1 Medical Bureau, Inc., Science Division, Burneice Larson, Chairman, 900 North Michigan Avenue, Chicago. BEST SOURCE FOR BEST SCIENTIFIC PERSONNEL. X

Scientific Illustrator experienced in all fields of black/white and color photography, electronscopy, x-rays, teaching many years for government and universities desires change; steady position in science or industry. Excellent background. Gonzales, Box 733, Pittsburgh 30, Pa. X

POSITIONS OPEN

BIOCHEMIST
ENDOCRINOLOGIST

Recent Ph.D. or June candidate in biochemistry or physiology with experience in problems of intermediary metabolism and enzyme actions. Must be self motivated and able to direct others in research dealing with the metabolism and mode of action of steroids, hormone, and agents for the control of biological fertility.

WRITE TO: PERSONNEL DEPT.

ORTHO PHARMACEUTICAL CORPORATION

ROUTE 202, RARITAN, NEW JERSEY

BIOLOGIST

M.S. or equivalent. Dynamic eastern pharmaceutical company seeks young scientist with sound training in virology and tissue cell culture or related fields, to participate in newly organized project in chemotherapy of virus diseases. Send résumé and references to

Box 225, SCIENCE

Chief of Pediatrics for internationally known chest hospital. Pediatric service now 50 beds, to be expanded to approximately 125 beds. Includes tuberculosis, cardiac disease amenable to surgical intervention, asthma, cystic fibrosis, and other chest entities. Active research, teaching, and rehabilitation programs. Mail curriculum vitae to Dr. S. Dressler, Chief of Staff, National Jewish Hospital, 3800 East Colfax Avenue, Denver, Colorado. 1/6, 13, 20

POSITIONS OPEN

(a) **Director, Publications and Public Relations**; prefer scientific background; must be effective in dealing with various outlets, medical, scientific researchers; supervise medical writers, staff members; prominent research institute; East. (b) **Bacteriologist**, M.S. and hospital experience required to head department, new 350-bed California hospital; $6000; coastal resort area. (c) **Biochemist**; M.S., Ph.D., to head modern department, 300-bed general hospital; to $10,000; industrial city near Chicago. (d) **Biochemist**; Ph.D. to assist in departmental reorganization; 300-bed voluntary hospital in lovely southeastern city; $12,000. (e) **Bacteriologist**; M.S., equivalent to direct department; general hospital 250 beds; $7500; Chicago suburban location. (f) **Pharmacologist**; Ph.D. experienced investigation autonomic drugs, able conduct independent research, supervise technicians; rapidly expanding California pharmaceutical company; to $12,000. (g) **Biochemist**; M.S., Ph.D., to supervise department; laboratory directed by two pathologists; 300-bed general hospital; $10,000–$12,000; Mideast. (h) **Bacteriologist**; excellent opportunities for recent graduates in state public health laboratory; northwestern capital city. (i) **Biochemist**; Ph.D. preferred to head department, very large general hospital; $10,000; southwestern university city 200,000. (j) **Bacteriologist**; B.S., M.S., trained pathogenic bacteriology for research in area anti-infective agents; to $7500 for M.S.; prominent midwestern pharmaceutical company. (k) **Chemists**; Ph.D.'s; one qualified organic chemistry, one biochemistry for research enzymes, enzyme metabolism as allergy related; to $13,000; outstanding eastern company. Science Division, Woodward Medical Bureau, Ann Woodward, Director, 185 North Wabash Avenue, Chicago. X

Medical Writer-Editor

Unusual opportunity for scientifically trained or experienced medical writer. Professional position with Ethical Pharmaceutical Division of expanding chemical corporation located in New York City suburbs. **Box 230, SCIENCE.**

(a) **Organic Chemistry Director** with imagination and leadership abilities to supervise section of rapidly expanding drug firm; Midwest. (b) **Bacteriologist** to head department of hospital recently expanded to 650 beds with excellent facilities; around $10,000; Southwest. (c) **Gross Anatomy Assistant Professor** for leading medical school; foreign. (d) **Pharmaceutical Chemist** with good biochemistry background for tableting, biological preparation, product control, and research for drug unit of diversified firm; $9000 up; East. (e) **Biologist** for teaching and research at vocational college; South. (f) **Parasitologist** qualified in histopathology-immunology as scientific associate to research director at leading medical institute; around $10,000; Midwest. (g) **Pharmacologist** for research on new chemicals and activity evaluation for drug firm; around $10,000; Midwest. (h) **Dairy Technologist** to direct new laboratory and vitamin fortification of dairy products program; $10,000–$12,000; East. (i) **Biochemist/Biologist** for studies of nucleic acid metabolism at cancer research hospital; around $9000; Southwest. (Please write for details; also many other positions available through our nationwide service.) S1-1 Medical Bureau, Inc., Science Division, Burneice Larson, Chairman, 900 North Michigan Avenue, Chicago. THE BEST SOURCE FOR THE BEST SCIENTIFIC POSITIONS. X

Ph.D. for Basic Research in Cystic Fibrosis. Field of interest—mucous synthesis on cellular level, analyses of body secretions and enzyme kinetics. Knowledge of use of isotopes helpful. Time for other work in field of personal interest. New research facilities. Excellent salary.

Box 2, SCIENCE

Research Assistantships in Biochemistry and Physiology at B.A. or M.S. level. Research applicable toward Ph.D.

Heart disease research institute associated with large midwestern university. Initial stipend up to $4800 for 12 months' service. Send complete résumé.

Box 1, SCIENCE

POSITIONS OPEN

PHARMACOLOGIST

Ph.D. or equivalent with experience in various fields of cardiovascular evaluation of new drugs. To head cardiovascular section. Send résumé to Charles R. Thompson, Director of Pharmacology, **Cutter Laboratories,** 4th & Parker St., Berkeley, California.

THE UNIVERSITY OF LIVERPOOL

Applications are invited for Imperial Chemical Industries Research Fellowships in Physics, Chemistry, Biochemistry, Engineering, Metallurgy and Pharmacology or any related subjects. Appointments will date from 1 October 1961. The salary will depend upon qualifications and experience, but will normally be within the range £700–£1,000 per annum, together with F.S.S.U. benefits and family allowance.

Applications, three copies, stating age, details of qualifications and experience, publications, and research work in progress and completed, together with the names of two referees, should be received not later than **11 February 1961**, by the Registrar, from whom further particulars may be obtained. (Candidates overseas who find it more convenient to do so may send one copy only by air-mail.) Quoting Ref CV/s.

The Market Place

BOOKS • SERVICES • SUPPLIES • EQUIPMENT

BOOKS AND MAGAZINES

Your sets and files of scientific journals

are needed by our library and institutional customers. Please send us lists and description of periodical files you are willing to sell at high market prices. Write Dept. A3S, CANNER'S, Inc. Boston 20, Massachusetts

PROFESSIONAL SERVICES

WISCONSIN ALUMNI RESEARCH FOUNDATION

LABORATORY SERVICES
for the FOOD, FEED, DRUG and CHEMICAL INDUSTRIES
Analyses, Biological Evaluation, Toxicity Studies, Insecticide Testing and Screening, Flavor Evaluation.
Project Research and Consultation
Write for Price Schedule
P. O. Box 2217 • Madison 1, Wis.

BIOLOGICAL SERVICES
Foods, Drugs, Cosmetics, Chemicals, Feeds, Packaging—Toxicological, Mycological and Bacteriological Investigations
United States Testing Co., Inc.
1415 Park Ave., Hoboken, N. J.

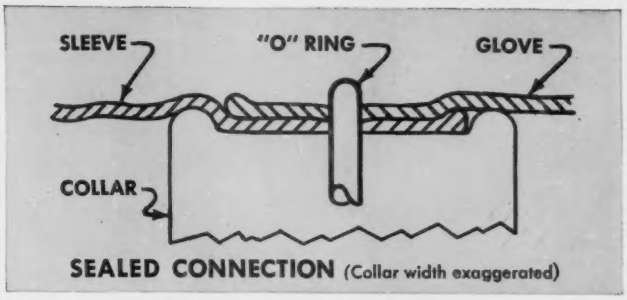
SUPPLIES AND EQUIPMENT

• HYPOPHYSECTOMIZED RATS
Shipped to all points via Air Express
For further information write
HORMONE ASSAY LABORATORIES, Inc.
8159 South Spaulding Ave., Chicago 29, Ill.

YOU NEED THIS FREE CATALOG FOR YOUR FILES
Serums, antiserums and bloods of all kinds for technicians and tissue culture laboratories. No salesman will call.
COLORADO SERUM CO.
4950 York St. • MAin 3-5373 • Denver 16, Colo.

from the originator of Berkeley Box gloves...

a decisive BREAKTHROUGH in the DRY BOX field!



SEALED CONNECTION (Collar width exaggerated)

WIL-GARD

Interchangeable **Berkeley Box** Sleeve and Glove Combination

Imagine—anyone can use your Berkeley Box facilities without changing sleeves! Work in a controlled atmosphere is now simplified by these new sleeves and interchangeable gloves. Most Wil-Gard industrial gloves up to 11-inches long can be mounted on a special collar attached to the sleeve which remains permanently flanged to the box. Changeover is made in seconds! Pin-holed or contaminated gloves can be quickly interchanged individually without replacing the sleeve—saving you money, time and manpower.

Hand temperature suppressors are molded to the inside surface of each sleeve and provide continuous circulation and change of fresh air, minimizing dew-point fluctuations inside the Berkeley Box.

No matter what you handle—radioactive materials, noble gases, chemical dusts, radioisotopes, reactor fuels, or analytical laboratory tests—this new combination makes a perfect team for your Berkeley Box needs!

All of these Wil-Gard Industrial Gloves, up to 11-inch, will fit our "Berkeley Box" Sleeves:

NATURAL RUBBER • SOFT-LINED LATEX • UNLINED LATEX • SOFT-LINED BLACK NEOPRENE • UNLINED BLACK NEOPRENE • UNLINED WHITE NEOPRENE • BUNA-N

Write for free descriptive literature.

SOLD ONLY THROUGH DISTRIBUTORS

PROTECTION FOR THE HANDS OF INDUSTRY

WIL-GARD

THE WILSON RUBBER COMPANY INDUSTRIAL DIVISION CANTON 6, OHIO

A Division of Becton, Dickinson and Company • Pacific Coast Warehouse: 530 Howard St., San Francisco 5, California

Wil-Gard and Berkeley Box are Trademarks of The Wilson Rubber Co.

WR-1160-77

She's Sharpening Knives...

That's right...she's sharpening microtome knives with AO's New Automatic Microtome Knife Sharpener while she busily cuts sections.

You're looking at a perfect team in action... a skilled technician using the famed "820" Microtome and the New AO Knife Sharpener. This combination assures complete control over all the factors necessary for cutting consistently uniform serial sections.

The AO Knife Sharpener provides on-the-spot facilities for honing and polishing knife edge and bevel. Operation is automatic; place knife in holder...set timer...flip the switch. The unit stops automatically when sharpening cycle is completed. There's never any need for further hand-honing or stropping.

You always have sharp knives on hand to assure the optimum sectioning results that the "820" Microtome is designed to produce.

Ask your AO Sales Representative to show you how little it costs...to put this unexcelled sectioning team to work for you... to help you reduce expensive knife inventories and outside servicing.

For further information or a convincing demonstration...write now.

American Optical Company

SPENCER

INSTRUMENT DIVISION, BUFFALO 15, NEW YORK

Dept. 0-1

☐ Please send further information on AO's sectioning team . . . "820" Microtome and New Model 935 Automatic Knife Sharpener.

☐ I would be interested in a demonstration.

Name_____

Address_____

City_____ Zone_____ State_____

IN CANADA write—American Optical Company Canada Ltd., Box 40, Terminal A, Toronto, Ontario